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Estimular a los grupos de trabajo existentes en Latinoamérica, sean investigadores, productores, funcionarios o simplemente interesados en las plantas medicinales y aromáticas, poniendo a su disposición este Boletín para la difusión y la divulgación de sus investigaciones y de las actividades que en general desarrollen en torno a plantas.

Ser una herramienta de difusión para la Sociedad Latinoamericana de Fitoquímica, principalmente, y de otras sociedades y agrupaciones que se sientan representadas por este Boletín.

Constituir un nexo entre los profesionales de habla hispana, francesa, portuguesa e inglesa de la región, relacionados con el tema central del Boletín

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Gracias de antemano por sus contribuciones

El comité editorial de BLACPMA

Editorial

Estimados lectores,

A todos nosotros nos une la pasión por las plantas medicinales pero también la preocupación por su futuro regulado y sostenible. BLACPMA pretende ser un foro de comunicación, actualización y discusión de todos los profesionales implicados en el cultivo de plantas medicinales y la investigación, desarrollo y producción de medicamentos herbarios.

Por tanto es misión obligada de este su boletín acometer, de vez en cuando, una auditoria de la situación del sector. Para ello el comité editorial de BLACPMA ha decidido abordar la situación actual de la regulación de los medicamentos herbarios (o fitomedicinas) en forma de números monográficos, para los cuales hemos invitado a autores de todo el mundo a explicar los últimos desarrollos reguladores en las distintas áreas geográficas y económicas de su competencia.

Para empezar en esta primera entrega se recoge la particular visión de las plantas medicinales de un referente mundial en el tema, Geoffrey Cordell, quien además de Profesor Emérito de Farmacognosia en Chicago, es activo miembro del comité de este boletín (Cordell, 2007).

Un primer bloque trata de enmarcar el tema con una somera visión de los movimientos pasados y actuales a nivel regulador regional y global (Prieto, 2007) a lo cual sigue una presentación de la situación europea como primer ejemplo mundial de regulación transnacional en materia de medicinas herbarias (Peschel, 2007a) y una discusión de las peculiaridades nacionales a la hora de implementar (¡o no!) estas directivas (Peschel, 2007b). Los dos autores trabajamos en el Centro de Farmacognosia y Fitoterapia de la Universidad de Londres que ha tomado un papel *leader* en la organización de encuentros sobre la regulación de Medicinas Tradicionales Herbarias Europeas (Heinrich, 2007).

Dos artículos sobre la situación reguladora de MH en Jamaica (Robertson, 2007) y Cuba (Ramírez *et al.*, 2007) proveen una excelente perspectiva de la diversidad de aproximaciones normativas en la Región del Caribe. Las autoras trabajan todas activamente en la regulación de MH en sus respectivos países a nivel privado e institucional respectivamente.

Para cerrar este número, el Profesor Mukherjee, editor regional en Asia de *Journal of Ethnopharmacology*, y sus colaboradores nos explican como el subcontinente Indio trata de establecer un marco único para la multitud de sistemas tradicionales que esta zona alberga así como las miles de plantas medicinales y drogas minerales y animales que forman parte de los mismos. Es un buen ejemplo de lo complejo que puede llegar a ser poner orden y concierto en un campo tan rico y diverso como la medicina tradicional.

En una próxima entrega trataremos de hablar de Sudamérica y Centroamérica, Norteamérica (México, Estados Unidos y Canadá), China y África. Esperamos que este en sus manos antes de Mayo próximo.

Aprovecho para invitarles a visitar nuestra página Web, que acorde al cambio del boletín ha crecido en complejidad. Ahora cuenta con servicios de búsqueda interna y descarga de separatas, entrega electrónica de artículos para su publicación, noticias y mucho más.

Sin más preámbulo, les dejo con la esperanza de que encuentren útil e informativo todo este material que hemos preparado con nuestra mayor ilusión.

Les saluda cordialmente,

Dr. José Maria Prieto
Coordinador del Especial Regulación de Fitomedicamentos
Editor Científico Jefe de BLACPMA

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Especial Regulación de Fitomedicinas / Special Issue on Regulation of Phytomedicines

A vision for medicinal plants

[Una visión de las plantas medicinales]

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Abstract

In the past few years, the author has written a number of articles discussing a vision for the development of medicinal plants. This article will therefore present only a brief synopsis of some of the more salient features of those articles, resulting in the presentation of four, clear, coalescing visions for the future of medicinal plants: enhanced quality control, sustainability for medicinal plants, pharmacognosy in a suitcase, and finding a strong "voice" at the political table of global health care.

Keywords: medicinal plants, regulatory affairs, pharmacognosy, quality control, sustainability, global health care.

Resumen

En el pasado pocos años, el autor ha escrito un cierto número de artículos en los que discutía su visión del desarrollo de la ciencia y regulación de las plantas medicinales. Este artículo pretende hacer una síntesis de algunas de las características más salientes de esas visiones de los artículos, dando por resultado la presentación de cuatro claras y complementarias visiones para el futuro de plantas medicinales: control de calidad realzado, sostenibilidad para las plantas medicinales, farmacognosia "en una maleta", y encontrar una "voz fuerte" en el campo de la política del cuidado médico global.

Palabras clave: medicamentos herbarios, farmacognosia, regulación, control de calidad, desarrollo sostenible, cuidados médicos globales.

In the past few years, the author has written a number of articles discussing a vision for the development of medicinal plants (Cordell, 2000; 2002; Cordell and Colvard, 2005; 2007). This article will therefore present only a brief synopsis of some of the more salient features of those articles, resulting in the presentation of four, clear, coalescing visions for the future of medicinal plants in global health care.

In "*A Still Forest Pool*" the venerated Thai monk, Ajahn Chah opined that "If you are on the fifth step and you think that you are too high, you will never make it to the sixth step". What I believe that he is saying, at many different levels, is there is always room for improvement, and don't be so complacent as to think that all is known that can be known, or that the best that can be done is being done. It is a philosophy that later came to be known in western management parlance as continuous quality improvement (CQI), questioning how further improvement of a system was possible. In my view, as far as medicinal plants in public health care globally are concerned, we are just beginning to LOOK at the first step. Yes, it is a public health care issue, although in some countries it is not seen that way, and thus the paucity of effective local regulations based on science. A recent WHO survey showed that of the 192 countries surveyed only 53 had any form of regulations for traditional medicines, and for only 18% of the countries were medicinal plants included in the National Pharmacopoeia (WHO, 2002). Yet, at least 64% of the global population use medicinal plants as their primary form of health care (Farnsworth et al., 1985), and this percentage will rise steadily as the global population reaches 10 billion in the next 30 years.

The lack of attention to the regulation of medicinal plants has occurred for a number of reasons, two of which are that: i) it is often assumed that these

medicinal agents, because they have been used for hundreds or thousands of years, are safe (and thus don't need regulation), and ii) their supply is unlimited. These are both myths which need to be dispelled.

As we think about the future of medicinal plants in health care, there are two burgeoning issues to be addressed: quality control and sustainability. For most of the countries of the world, pharmaceutical companies will not be providing the medicinal agents for local prevalent diseases, and for those diseases that are global, the drugs are likely to be very expensive. The question for these health care systems is how to address those issues, for optimum local health care. Medicinal plants, all over the world, are sold in a manner which has changed little in hundreds, may be thousands, of years. That is not something medicinal plant scientists should either be proud of, or condone. Quite the reverse, they should be irate that their science is having such a limited impact on public health.

From a public health perspective, what is a reasonable time frame to enhance quality control through the application of science and technology to traditional medicine? What can be done in 5 years, what in 10 years, and what in 15 years? Can a strategic health care plan which incrementally enhances the safety and effectiveness of traditional medicines for the benefit of the patient be developed? Where do we start to make these improvements? What are the sciences and the technologies that need to be involved? Are there enough scientists locally who are trained to do the work? Are governments prepared from a regulatory and science enforcement perspective? And of course, who will fund all those studies and protocol developments?

This is not the place to be addressing in great detail all of the steps to achieve a safe and efficacious traditional medicine, but a brief overview is presented (Cordell, 2000; Cordell and Colvard, 2005): i) All research programs begin with a **literature evaluation**. In the field of medicinal plant research, one of the highest priorities must be the determination of what is known and what questions need to be answered with a view to not duplicating previous research and wasting precious human and fiscal resources; ii) It is rare indeed that ethnomedical research is conducted with the **scientist and clinician doing field evaluations** of particular remedies using standardized clinical evaluation methodologies. Such strategies will markedly enhance the veracity of medicinal plant claims; iii) Plants are complex factories for secondary metabolites. A **determination of the active principle(s) and their mechanism of action** is critical for the development of systems for chemical and biological standardization; iv) Given the diversity of medicinal plant materials that are now in global commerce, it is critical that there be analytic standards in place to **eliminate contaminants and adulterants** which might pose a health hazard, are illegal, or which give a non-reproducible, false biological responses; v) Standardization of a given preparation for the patient should be based on a three-fold **botanical, chemical, and biological standardization** so that on a lot-to-lot basis there is a safety and efficacy guarantee for the patient. Botanical standardization based on PCR analysis, chemical standardization based on a known active principle (or principles), and biological standardization based on a cheap, relevant, and validated *in vitro* bioassay; vi) The age of a traditional medicine is an important issue, but is rarely given. For each preparation there will need to be **stability and safety studies**, since it cannot be assumed that a preparation that has been used for hundreds of years is necessarily "safe". Neither can it be assumed that the active principles, and therefore the clinical effectiveness of the product, will be stable for the shelf life of the product; vii) These botanical, chemical, biological, and stability studies should culminate in a **demonstration of clinical effectiveness** for a well-defined, standardized preparation in an appropriate clinical trial; viii) There is the need to report and **register observed plant drug – drug interactions** which occur. Some of these may be adverse interactions causing unwanted side effects, while others might be synergistic interactions causing potentiation of activity, and requiring dose modulation; ix) Finally, there is the need for sustainable development of a commercial medicinal plant.

The forests and the mountains are already being depleted of medicinal plants as demand increases; and many desirable medicinal plant species are now listed as endangered in their native habitats. Relatively little attention is being given to this aspect of medicinal plant development because the science to discern which plants are the most effective has not yet provided priorities for sustainable development. As the UN Millennium Ecosystem Assessment indicates (Millennium Ecosystem Assessment, 2005), we can no longer assume that the plant materials that are used as resources today will be there tomorrow. Consequently, and if the world is to have plant-based

medicinal agents in the future for a rapidly expanding global population, we must think of plant-based drugs as a fundamental health care requirement. For continued availability, we must therefore regard an effective medicinal plant as a sustainable, renewable resource; a **sustainable drug**. For most people that is a new concept; many medicinal plant scientists do not think in those terms.

New strategic thinking is also needed as to how medicinal plants are initially validated. We need to consider how to reverse the paradigm of collecting medicinal plant materials, identifying them macroscopically, drying them, bringing them back to the laboratory, extracting them, and testing the extracts for biological and pharmacological activities. Supposing the "laboratory", the techniques needed to accomplish all of the steps just described, was taken to the field, and the preliminary determination regarding a level of interest for further experimentation made on site. Is there the potential to determine the authenticity and the chemical and biological potential of a medicinal plant *in the field*? What are the implications for future studies of medicinal plants if that strategy can be successful? What are the range of technologies that need to be assembled for the botany, chemistry, and biology to be conducted? What are the nano technologies which can be applied to realize this? What areas of the required technologies need further development? Are there other barriers to the realization of this goal? What would "pharmacognosy in a suitcase" look like?

These are my three very clear visions for medicinal plants: enhanced quality control, sustainability for medicinal plants, and pharmacognosy in a suitcase. They are significant regulatory, scientific, technological, economic and social challenges. They will take many years to accomplish, and many people to educate about the validity and absolute need for the approach. That brings me to my fourth vision... which is that medicinal plants, and their study for the future of the health of humankind, will find a strong "voice" at the political table of global health care for the sake of future generations.

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Especial Regulación de Fitomedicinas / Special Issue on Regulation of Phytomedicines

La regulación global de los medicamentos herbarios

[The global regulation of herbal medicines]

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Abstract

This paper gives an overview on the regional and global regulatory efforts towards a homogenization of the normative about herbal medicines. The pioneering work of the WHO and the recent implementation of the first transnational directive on herbal medicines in Europe have laid the legal and scientific foundations to help a fast implementation of transnational regulations elsewhere. The most advanced regional frameworks are those of Latin America and the Asiatic east. China has started a process of internal regulation to facilitate the globalisation of its traditional medicinal system. Africa is working towards the regulation of the traditional medicines as a previous step to their transnational regulation. If a global regulation for herbal medicines is still far away, several organisations already started this process by introducing this subject into the agenda of the periodic meetings of national regulatory agencies all around the world.

Keywords: Globalisation, transnational regulations, herbal medicines, regulatory affairs.

Resumen

Se pretende presentar una visión conjunta de los esfuerzos regionales y globales para homogeneizar las normativas relativas a la regulación de medicamentos herbarios. El impulso inicial dado por los trabajos de la OMS y el ejemplo de la primera regulación trasnacional, en la forma de la Directiva de Medicinas Tradicionales Europeas, han sentado las bases documentales científicas y legales para ayudar a una rápida implementación de medidas trasnacionales en otros continentes. La implementación de distintos consensos regionales sobre esta materia esta muy avanzada en Latinoamérica y el Este Asiático. China ha emprendido un camino de implementación de normativas que le permitan la globalización de su sistema de medicina tradicional. África trabaja intensamente en la regulación a nivel nacional de las medicinas tradicionales como un paso previo a su regulación transnacional. Sin bien una regulación global tardará en conseguirse, diversos organismos ya han emprendido este camino en forma de encuentros regulares entre agencias reguladoras de todo el mundo.

Palabras clave: Globalización, regulaciones trasnacionales, medicamentos herbarios, regulación.

INTRODUCCION

Las medicinas herbarias (MH), o si se prefiere fitomedicinas, están mas que nunca en el ojo regulador de naciones, organizaciones trasnacionales y entes internacionales. En casi todo el mundo las legislaciones nacionales se encuentran bajo una doble presión: la de un público que demanda mayor calidad en los productos, y la de los responsables de salud pública que exigen mayor seguridad.

Las grandes industrias del sector tienen diferentes posturas dependiendo del marco en que tradicionalmente se han movido: pasividad si gozan de mercados protegidos y afán regulador en espacios económicos abiertos a la competencia, sin olvidar que muchas ven en todo ello una oportunidad de reducir la competencia de las pequeñas compañías que no podrán afrontar los altos costes derivados de la elevación de los remedios herbarios a la categoría de 'medicamento'. Hay que resaltar el hecho de que el concepto de medicamentos herbarios esta destinado a situarse dentro de una línea 'blanda' de registración, donde se exige una calidad garantizada pero no una eficacia probada científicamente.

El factor clave desencadenante del vendaval regulador ha sido la exitosa globalización de las medicinas tradicionales y complementarias (MT/MC). Hoy en día se consumen productos procedentes de la Medicina Tradicional China (MTC) o Ayurveda o europea o sudamericana e incluso africana en casi todos los países desarrollados, generando una demanda creciente del mercado a nivel mundial. Aquí es donde resalta por su ausencia una regulación internacionalmente homogénea: en los países de origen hay generalmente falta de

información sobre el productor, y además no existe comunicación entre las agencias reguladoras nacionales de países exportadores e importadores, todo ello creando una constante fuente de problemas para los servicios aduaneros y sanitarios en todo el mundo.

Muchos países han comenzado ya la regulación de sus mercados nacionales de MH mediante enmienda de sus leyes. La mayoría de ellas datan de los años sesenta y setenta y entonces casi ninguna contemplaba la categoría de MH. Otros países no parecen tener mayor preocupación por establecer una categoría aparte para lo que hasta ahora se comercializa principalmente como suplemento alimentario, EE.UU. por ejemplo.

Existen numerosos desarrollos de regulación de medicamentos a niveles subregionales y regionales, algunos ligados a la creación de espacios económicos comunes. Sin embargo el nivel de actividad reguladora en el campo de los MH dentro de cada una de ellas varía considerablemente. Entre los cuales destacan:

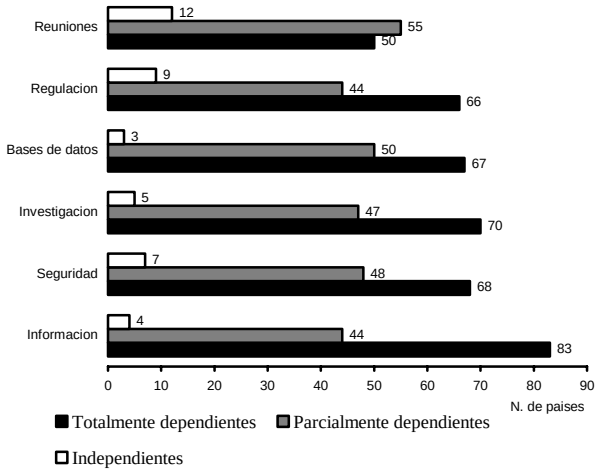
- Association of South-East Asian Nations (ASEAN)
- Andean Community (CAN)
- Collaboration Agreement of Drug Regulatory Authorities in European Union Associated Countries (CADREAC) – most (10) countries involved entered EU in 2004
- European Union (EU)
- Gulf Cooperation Council (GCC)
- International Conference on Harmonisation (ICH)
- International Conference of Drug Regulatory Authorities (ICDRA)
- MERCOSUR (Southern Common Market)
- Pan American Network on Drug Regulatory Harmonization (PANDRH)
- Southern African Development Community (SADC)
- Cada una de las seis regiones de la OMS

Los principales problemas que afrontan las autoridades a la hora de regular el sector de MH son la falta de datos científicos, la falta de mecanismos efectivos de control, y la falta de educación, formación y especialización del personal relacionado con la producción, distribución, prescripción, uso y seguimiento del uso de MH (Zhang, 2006).

LA OMS COMO FUENTE REGULADORA GLOBAL

Tras el reconocimiento por parte de la OMS del valor de la medicina tradicional como fuente de salud y de biodiversidad en la Conferencia de Alma Ata de 1979 (OMS-UICN-WWF, 1993; OMS, 2002), se han venido financiando grupos de trabajo internacionales y regionales, así como proyectos locales, para estudiar y fundamentar su uso regulado (WHO, 2001, 2005), la redacción de monografías de control de calidad (WHO, 1998), de buenas prácticas agrícolas (GAP) (OMS, 2003), de buenas practicas de producción (GMP), de normas para asegurar la seguridad de los productos herbarios (WHO, 2004a), y de estrategias para su correcto uso en los sistemas de salud primarios (WHO, 2004b). Muchos países en vías de desarrollo han podido regular las medicinas herbarias en sus respectivos territorios nacionales basándose en este cuerpo documentario, lo cual hubiese sido imposible desarrollar únicamente a nivel local. De hecho la necesidad del impulso de la OMS hoy en día es aun altísima, con solo un mínimo de países realmente autosuficientes para regularse como muestra la Figura 1 (Zhang, 2006).

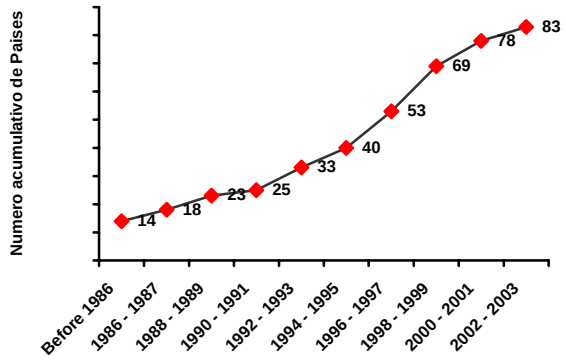
Figura 1. Dependencia de la OMS en cuanto a regulación de MH (Zhang, 2006).



Leyenda: Reuniones (Congresos globales sobre regulación); Regulación (Talleres sobre regulación de MH); Bases de Datos (Necesidad de bases de datos con información sobre MH); Investigación (Guías generales de investigación de la eficacia de MH); Seguridad (Talleres sobre seguimiento de la seguridad de MH); Información (Necesidad de reuniones para intercambio de información sobre asuntos de regulación)

La OMS realizo dentro de este contexto un informe sobre el estado de cada una de las legislaciones nacionales de 141 países sobre MT/MCA (WHO, 2004c, 2005). El resultado fue que el 65% de los países consultados disponían de regulación de TM/CAM y el 42% están en el proceso de regulación. La evolución en los últimos tiempos puede observarse en la Figura 2.

Figura 2: Numero de países con legislación Nacional sobre regulación de MH o TM/CAM (WHO, 2004; 2005).



REGULACION TRASNACIONAL EN AMERICA

Se están llevando a cabo distintas iniciativas regionales y continentales para llegar a una homogenización de categorías y características de los distintos productos herbales de consumo humano en América. Por un lado la Organización Panamericana de Salud (OPS o PAHO) auspicia encuentros regulares entre los responsables reguladores de los distintos países del continente. Por otro lado existen múltiples iniciativas regionales a cargo de asociaciones de libre comercio como MERCOSUR, ANDEAN, y CARICOM por ejemplo.

Mercosur

MERCOSUR cuenta como miembros de pleno derecho Argentina, Brasil, Paraguay, Uruguay y Venezuela, mientras que Bolivia, Chile, Colombia, Ecuador y Perú son estados asociados y México y Nicaragua estados observadores.

En este espacio común económico se vienen realizando diversas reuniones bajo el nombre de MERCOFITO donde se debaten todos aquellos aspectos relacionados con la incorporación de fitomedicamentos en los sistemas de salud, el desarrollo de polos productivos regionales a través de la incorporación de cultivos de plantas medicinales, la posibilidad de crear una Farmacopea del Mercosur para este tipo de productos, mostrar los trabajos científicos así como coordinar ensayos clínicos en la región, sin olvidar la implementación de estrategias para concienciar a la población sobre el uso racional de este recurso, y debatir políticas regionales en común para la enseñanza en foros académicos de la Fitomedicina en consonancia con los enunciados propuestos por la Organización Mundial de la Salud. Para una descripción mas detallada de sus objetivos ver Cuadro 1) (Mercofito, 2007).

Mercofito esta compuesto por diversos entes tanto gubernamentales como privados, incluyendo Ministerios de Salud del Brasil, Argentina y Paraguay, agencias nacionales como la Agencia Nacional de Vigilancia Sanitaria de Brasil (ANVISA), instituciones académicas (Universidad Nacional de Asunción) y profesionales (Asociación Argentina de Fitomedicina) así como diversas organizaciones locales como por ejemplo el Comité Gestor de Plantas Medicinales de Itaipú Binacional, Fórum por la Vida – Proyecto Plantas Vivas de la Asamblea Legislativa de Rio Grande do Sul (ALERGS), ONG Agración, Asociación del Centro Integrado de Educación, Naturaleza y Salud (ACIENS-Brasil).

Caribe

La región caribeña tiene plena conciencia de que sus productores y ciudadanos en general están poco o nada capacitados para beneficiarse de sus recursos locales debido a una falta tanto de visión como de inversión. Los principales problemas económicos que impactan negativamente sobre la industria herbolaria caribeña son: intercambio con el extranjero limitado, poca tasa de empleo y poca capacitación de la industria local, pobreza, poca especialización en la mano de obra, ausencia de colaboración entre sectores económicos clave y falta de estructuras para el transporte de mercancías entre las Islas de la región (Robertson, 2007a).

La situación a nivel regional es muy complicada. Cuba lleva a cabo una intensiva implementación de los medicamentos herbales en su sistema de salud para paliar las consecuencias de una difícil situación internacional. Entre el resto de Islas de habla hispana no existe ninguna actividad intergubernamental sobre el tema digno de mención aparte de la llevada a cabo dentro de los foros regionales de la OMS u OPS.

Cuadro 1. Propuestas y objetivos de MERCOFITO.

- Elaboración de una Farmacopea Herbaria del Mercosur, que permita el rescate del conocimiento tradicional sumado al aporte del conocimiento científico.
- Incorporación de la enseñanza de la Fitoterapia dentro de las disciplinas obligatorias de grado y posgrado en las carreras universitarias del área de la salud, así como la enseñanza de la misma como asignatura dentro de los planes de formación entre los agentes de atención primaria de la salud. La propuesta de enseñanza sobre plantas medicinales comprenderá también las áreas de enseñanza universitaria de las carreras agrarias, sociales, ambientales y antropológicas. Se debatirá, además, crear una Universidad del Mercosur donde puedan desarrollarse carreras relacionadas con las áreas antes descritas.
- Creación de la Red Mercofito – una red de cooperación técnico-científica – integrada por gobiernos, universidades, laboratorios nacionales, asociaciones profesionales, fundaciones y empresas con compromiso social pertenecientes al Mercosur, cuyo objetivo será priorizar la cadena productiva y el desarrollo socioeconómico regional a través del cultivo de plantas medicinales y elaboración de medicamentos fitoterápicos. A su vez, se propone crear un Fondo de Investigación, Producción y Formación de Recursos Humanos, por medio de los diferentes integrantes de la red.
- Elaboración de una política en común consensuada sobre plantas medicinales y medicamentos fitoterápicos entre los países integrantes del Mercosur (socios activos y adherentes). Se propone la creación de un Ente Coordinador sobre Plantas Medicinales para cada país miembro (a excepción de aquellos países que ya lo tengan). Asimismo, los diferentes Ministerios de Salud de cada país establecerán las medidas necesarias para la incorporación de medicamentos fitoterápicos en los Vademécums de Remedios, así como las políticas necesarias que tiendan a incorporar este tipo de recurso en los centros de Atención Primaria de la Salud.
- Integración entre los Ministerios de Relaciones Exteriores de los países miembros del Mercosur, para establecer pautas o criterios de trabajo para la toma de decisiones políticas inherentes a las experiencias de la cadena productiva de plantas medicinales y medicamentos fitoterápicos para el Mercosur.
- Tareas de coordinación y diálogo entre los integrantes del III° Mercofito y de PLANSUR con las Cámaras empresariales de fitomedicamentos y las entidades que nuclean al sector agrotecnológico de cultivo de especies medicinales, de manera tal que permitan fortalecer la cadena productiva agroexportadora de estos productos.
- Rescate y reconocimiento del patrimonio etnomédico correspondiente a los pueblos originarios de los países integrantes del Mercosur. Dentro de dicha pauta se propone incorporar a las distintas etnias al sector productivo para el desarrollo de polos agrícolas elaboradores de materias primas a partir de plantas medicinales.
- Elaboración de un Manual sobre Plantas Medicinales y Medicamentos Fitoterápicos para el Mercosur, el cual contemplará información de uso tradicional, validación científica de dichos usos, aspectos toxicológicos, galénicos, botánicos, indicaciones de uso y agrotecnología de cultivo de las especies incorporadas.
- Establecimiento de un Comité de Expertos que permita la optimización de la cadena productiva, por medio de la normatización de procedimientos que aseguren la calidad de la materia prima, la correcta selección de especies de acuerdo a las necesidades epidemiológicas y la preservación y manutención del germoplasma.
- Generar los marcos regulatorios adecuados para armonizar aspectos legislativos, asistenciales, técnico-científicos, comerciales y sobre propiedad industrial (Ley de Patentes).

Las islas anglófonas son mas activas y ya están organizadas y sensibilizadas sobre el tema. Como primer paso se realizo un estudio sobre las especies caribeñas de mayor importancia industrial para una primera fase de explotación financiado por el CTA (Centre for Technical Agriculture) en colaboración con Holanda y el IICA (Inter-American Institute for Cooperation on Agriculture). Por otro lado, se han creado dos asociaciones de carácter no gubernamental para propulsar la coordinación a nivel regional: la Caribbean Association of Researchers & Herbal Practitioners (CARAPA) y Caribbean Herbal Business Association (CHBA).

CARAPA, que se creo en 1998, esta formada por herbolarios, científicos y personal sanitario y pretende integrar el sistema tradicional en el sistema convencional de salud, con una especial preocupación respeto a eficacia, estudios clínicos y seguridad de su uso (CARAPA, web site).

Por su lado la CHBA pretende llegar a crear un grupo industrial operacional regional (*Industrial Cluster Operation)* para lo cual organiza talleres de trabajo para el control de calidad con la ayuda del CDE (Center for Development Enterprise) bajo el auspicio del ICS-UNIDO. A nivel legislativo se trabaja en la enmienda del actual marco legal para ponerlo a la altura de los tiempos y sacar de la desregulación al sector (Roberton, 2007a).

Iniciativas Latinoamericanas

Redes de trabajo internacionales como CYTED y RIPROFITO financian estudios de Legislación sobre Fitofármacos en América Latina como parte de sus Subprogramas, así como libros de monografías de plantas específicamente latinoamericanas (Gupta, 2003; García y Cáceres, 2000). Las conclusiones de dichos trabajos reflejan la enorme heterogeneidad en la terminología empleada para describir las especialidades herbarias, así como faltas importantes en el sentido de que a menudo no hay una clara definición de la materia prima y del principio activo, poca uniformidad en los requisitos de registro y

posterior comercialización así como enormes diferencias entre las normas de calidad, seguridad y eficacia. Para resolver estos desfases se trabaja en: Promover y fortalecer el intercambio de información sobre Plantas Medicinales; Promover la garantía de la calidad, seguridad y eficacia de Plantas Medicinales en las Américas, incluyendo el desarrollo de un programa de vigilancia y control; Desarrollar propuestas armonizadas en el tema de Plantas Medicinales: Apoyar a los países en la implementación de las mismas promoviendo programas y actividades de educación para proveedores de servicios de salud, consumidores y público en general (Gupta, 2003).

Iniciativas americanas de armonización de sistemas indígenas y convencionales

La armonización del espacio americano esta siendo facilitado por una iniciativa que en principio perseguía documentar y reconocer oficialmente los sistemas de medicina y terapia indígenas, asignándoles un puesto dentro de los respectivos sistemas de salud, lo que se ha denominado "Proceso de armonización de sistemas indígenas y convencionales". Desde 1993, la OPS ha trabajado en esta Iniciativa de Salud de los pueblos Indígenas. Primariamente tenía el objetivo de mejorar la salud y bienestar de dichas comunidades culturales. Sin embargo este trabajo esta derivando en la homogenización de políticas regionales para regular la medicina tradicional y con ella los medicamentos herbarios. En 1997 se culmino la primera etapa de este proyecto con las resoluciones CD37.R5 y CD40.R6 que apelan a los estados miembros a velar por soluciones sostenibles que tengan en cuenta las barreras geográficas, económicas y culturales de los grupos mas vulnerables, incluyendo los indígenas.

En 1999 la OPS/OMS organizo un grupo de trabajo en Medicinas tradicionales complementarias y alternativas como actividad conjunta de la División de desarrollo de Sistemas y servicios (HSP) y el departamento de políticas de drogas y medicinas esenciales. Los participantes recomendaron promover actividades para apoyar los conocimientos de medicina tradicional, complementaria y alternativa e identificar estrategias para contribuir a la organización y creación de sistemas de salud adecuados en toda América que reconozcan explícitamente la contribución a la salud pública de las medicinas indígenas. Para ello apelaron a la coordinación entre OPS/OMS y entidades de reconocido prestigio en medicinas tradicionales como la Universidad de Illinois en Chicago (UIC), EE.UU., y el Centro de medicina complementaria y alternativa del instituto nacional de salud (NCCAM-NIH).

Durante 2000-2001 se desarrollo una segunda fase del proyecto que focalizaba en la medicinas herbarias, Indígenas y las Tradicionales, Alternativas y Complementarias, con el objetivo de promover e integrar la medicina indígena en los sistemas de salud primaria. Ahora se trata de continuar los trabajos en estas áreas específicas dentro del marco de una Estrategia Global para la Medicina Tradicional, cuya culminación fue el 'global meeting' que tuvo lugar en Ottawa, Canadá (IRCH, 2005).

Todo este esfuerzo esta teniendo ya una traducción concreta a nivel de políticas nacionales. Argentina y Chile han consentido en la formación de personal especializado en medicina Mapuche y la creación de dispensarios de medicina tradicional Mapuche físicamente situados en los centros de salud públicos (Linares Calvo, 2007; Ylarri, 2007; Orrego Guerrero, 2002). Ecuador y Panamá podrían seguirlos en breve ya que llevaron a cabo estudios previos de documentación de la contribución de las medicinas y terapias indígenas en la atención de salud primaria y se diseñaron instrumentos y metodologías para entender la seguridad y eficacia de dichos sistemas tradicionales con la ayuda de la OPS (PAHO, 2002).

Iniciativas panamericanas

La Reunión del grupo de trabajo de la PAHO realizada en Curitiba (Brasil) (PAHO, 2006) hizo propuestas para avanzar en la homogenización del sector fitoterápico a nivel continental:

a. Propuesta de definición de Plantas Medicinales a ser adoptada por todos los países;

b. Propuesta armonizada de requisitos para plantas medicinales basada en criterios científicos;

c. Necesidad de asegurar la calidad, eficacia y seguridad de las plantas medicinales;

d. Promoción y educación para proscriptores y consumidores.

Sin embargo el peso de la actividad reguladora lo lleva sobre todo la Pan American Network for Drug Regulatory Armonización (PANDRH) que se dedica a identificar problemas en el desarrollo de la armonización global de regulación de todo tipo de medicamentos, incluidos los MH para facilitar lo que definen como "hemispheric drug regulatory harmonization". Esto se consigue siguiendo de cerca los desarrollos de grupos subregionales y recomendando estrategias y acciones. La PANDRH incluye reguladores de la Andean, Caricom, Mercosur, NAFTA, SICA, así como de la Industria y la

Academia. La regulación homogénea futura de los MH se incluyo dentro de las prioridades identificadas tras las tres conferencias realizadas en Washington (1997, 1999 y 2002) lo que sin duda refleja la importancia de estos productos en los mercados americanos (Molzón, 2003).

REGULACIÓN TRASNACIONAL EN AFRICA

Los intentos de regulación pan-africanos empezaron en 1985 con la redacción de una Farmacopea Africana en dos volúmenes bajo los auspicios de la Organization of African Unity Scientific Technical Research Commission (OAU/STRC) (CAMH, 2005). Con este cuerpo documental mas los producidos por la OMS, la OAU tomo la decisión en Julio de 2001 de declarar la primera década del s. XXI como la "Década de la Medicina Tradicional" (Ministers of Health of the WHO African Region. 2007). El Foro Africano para el Desarrollo (ADF) es una iniciativa conducida por la Comisión Económica Africana (ECA) para impulsar una agenda conducida por organismos netamente Africanos sobre programas específicos como la "Declaración de Abuja acerca de HIV/AIDS, Tuberculosis y otras enfermedades infecciosas" (African Development Forum, 2000).

Las tareas a afrontar son establecer pautas para la formulación, puesta en práctica, supervisión y evaluación de un marco jurídico para la práctica de la medicina tradicional en los diferentes países; establecer un código ético para su implementación en el sistema de salud; crear un marco regional para el registro de medicinas tradicionales y sobre todo un marco regulador para la protección de los derechos de propiedad intelectual y del conocimiento indígena de medicinas en la región del africana de la OMS (Kofi-Tsekpo, 2004).

La consecución de los objetivos previstos de la sensibilización de la década (2001 - 2010) y de la popularización de la medicina tradicional en todos los Estados miembros (CAMH, 2005) proveerá *de facto* las bases para una regulación continental de las MH. Aparte existen ciertas iniciativas a nivel sub-africano como la Southern African Development Community (SADC) que entre otras tareas coordina una parte del esfuerzo común de diversos países sudafricanos en frenar el SIDA dándole a la medicina tradicional un papel relevante.

1. Adopción de políticas nacionales sobre medicina tradicional.
2. Establecimiento de marcos jurídicos y de la legislación necesaria sobre medicina tradicional en todos los Estados miembros.
3. Adopción por parte de los Estados miembro de las herramientas de WHO/AFRO y de EMRO para institucionalizar la medicina tradicional en los sistemas de la salud.
4. Establecimiento de estructuras permanentes en los ministerios de la salud para poner en ejecución programas de medicina tradicional en todos los Estados miembros.
5. Inauguración de mesas nacionales de la medicina tradicional para regular su práctica y sus productos.
6. Adopción de políticas nacionales para la protección del acceso a la biodiversidad y del conocimiento médico tradicional (ley modelo del AU).
7. Establecimiento de centros de colaboración de excelencia/OMS para la investigación y el desarrollo de las medicinas tradicionales usadas para el tratamiento de las enfermedades prioritarias.
8. Institución en todos los Estados miembros de una semana nacional de la medicina tradicional.
9. Creación de el ambiente político, económico y regulador necesario para permitir el desarrollo de la producción local y la conservación de plantas medicinales y aromáticas.
10. Promoción de la investigación preclínica y evaluación clínica, desarrollo, producción local y comercialización de medicinas tradicionales estandardizadas.
11. Registro de medicinas tradicionales estandardizadas en la lista esencial nacional de medicinas tradicionales.
12. Prescripción, uso racional y supervisión de medicinas tradicionales estandardizadas en sistemas de cuidado médico públicos y privados.

Cuadro 2: Objetivos de la Década Africana de la MT.

REGULACIÓN TRASNACIONAL EN ASIA

Oriente Próximo

En noviembre de 2001, las autoridades reguladoras de los Estados miembros del WHO del Este de la Región Mediterránea se reunieron en El Cairo para discutir la regulación regional de las medicinas herbarias. Las medicinas tradicionales son ampliamente utilizadas en esta región pero la mayor parte de estos países no tiene ninguna ley sobre el control de calidad de medicinas herbarias. Algunos países, tales como la República Islámica de Irán, la República Árabe Siria y de Yemen, tienen monografías para las medicinas herbarias. Las preocupaciones de las autoridades reguladoras en la región se refieren generalmente más a la falta de seguridad en las MH que a su eficacia. Hay una gran necesidad de personal experto para controlar a los

productores de medicinas herbarias. Por tanto las prioridades regionales en el área de medicinas herbarias incluyen el entrenamiento de los profesionales de salud, la educación pública, el fomento de intercambio de información y la formación de expertos nacionales para registrar MH y auditar en GMP, sin olvidar la necesidad de referencias para las plantas medicinales traducidas a los lenguajes de la región y la creación de una estrategia de protección de los recursos vegetales. (Ren y Keller, 2002)

ASEAN

Los países de la Association of South-East Asian Nations (ASEAN) que son Brunei, Darussalam, Indonesia, Malasia, Filipinas, Singapur, Tailanda y VietNam (y en un futuro próximo Camboya, Laos y Myanmar) han creado un espacio común económico y están apostando fuertemente por la constitución de un polo biotecnológico regional estableciendo colaboraciones estratégicas con otros espacios económicos, empezando por Europa, lo cual se ha materializado en el ECAP (EC-ASEAN Intellectual Property Rights Co-operation Programme).

La ASEAN comenzó su esfuerzo integrador ya en in 1979. En la practica los primeros proyectos en el sector de medicamentos empezaron a implementarse hacia 1982, con la ayuda de WHO, UNDP y JPMA. Dentro de las múltiples actividades de homogenización de sus mercados farmacéuticos, la estandardización, control de calidad y uso de MH en la ASEAN es parte los objetivos generales del programa llamado ASEAN TCAC Pharmaceuticals que persigue reforzar el sector farmacéutico mediante el cumplimiento de las recomendaciones de la OMS/DAP y conseguir en la región una autosuficiencia en recursos humanos especializados.

El uso de MH en todos los países ASEAN se estimula por la necesidad de incrementar la cobertura de salud y por la de aprovechar los recursos locales en una región en la que el uso de MH es tan extendido e intenso. Para ello se constituyo el Traditional Medicines & Health Supplements Product Working Group (TMHS – PWG). Su primera prioridad ha sido la de obtener materiales de referencia como premisa para establecer las normativas y directrices de calidad, así como para atacar los problemas actuales de la región en materia de medicina tradicional que consisten principalmente en la proliferación de productos adulterados o falsificados, confusión de nombres, combinaciones de plantas con potencial efecto toxico, contaminaciones de metales pesados y uso no sostenible de plantas inmaduras.

Los resultados del esfuerzo común en ASEAN han sido la creación de un manual de cultivo, producción y uso de MH en la salud primaria, la concretización de acuerdos de elaboración de MH siguiendo GMP, la publicación de un primer volumen de 36 monografías de MH medicinales de interés regional, a lo que se suma la de otras 14 monografías de drogas crudas y la creación de mas de 40 herbarios a disposición de las autoridades locales. Los lideres de los países miembros de ASEAN acordaron que en 2010 las MH y suplementos dietéticos deben estar regulados en su espacio común (ASEAN, 2007a; 2007b; Zhang, 2006).

China - Europa

China quiere globalizar su sistema tradicional y asegurar que las políticas reguladoras en marcha en Europa y otros países no le cierren el paso a sus exportaciones de plantas medicinales. Para ello en 2005 ha actualizado la edición de su farmacopea bajo la supervisión de expertos europeos con el objetivo de acercar las normas de calidad chinas a los parámetros occidentales que hacen hincapié en la determinación de marcadores químicos y sustancias bioactivas. Este aspecto marca la evolución de la aproximación china clásica a la calidad del material vegetal que se basaba mas en la identificación del material y su procesamiento principalmente.

Por otro lado China y la Unión Europea han establecido un canal privilegiado para la regulación de las drogas vegetales usadas en la medicina tradicional china (MTC) con vistas a la homologación de las monografías de la farmacopea china que permitan su importación, venta y dispensación en Europa. Esta voluntad ha cristalizado en un reciente encuentro al máximo nivel en Roma (Ministry of Science and technology of RRPP China, Ministero Della Sanita de Italia, Directorate General for Research EU, 2007) y provee un segundo espacio común Sino-Europeo para los medicamentos herbarios.

Hong Kong, que siempre ha sido el punto de enlace entre China y el Occidente, se sitúa velozmente en este papel en cuanto a la globalización de la MTC se refiere. En esa ciudad se han creando distintas organizaciones para potenciar este proceso. Ejemplos son la Modernized Chinese Medicine International Association (MCMIA) formada por científicos y profesionales de la industria y que pretende poseer un fuerte carácter multi-disciplinar. El Consortium for

Globalization of Chinese Medicine (CGCM) creado en diciembre de 2003 agrupa a 19 instituciones de todo el mundo y pretende avanzar en las metodologías requeridas para el control de calidad de los MH aplicando las mas modernas tecnologías, crear una base de datos con información completa sobre MH chinos y coordinar ensayos clínicos de acorde a normas internacionalmente validas.

REGULACION TRASNACIONAL EN EL AREA DEL PACIFICO

Western Pacific Regional Forum for the Harmonization of Herbal Medicines (FHH)

La necesidad prioritaria de este grupo, compuesto por Australia, China, Japon, Republica de Korea, Singapur, Viet Nam y Hong Kong (SAR China) es el de regular la MTC, que es usada activamente en estos países con las mismas pautas filosóficas que en China. Sin embargo existe una disparidad de normas de calidad que impiden el comercio fluido de MH en la región (Zhang, 2006).

La FHH es un foro técnico en el que participan las autoridades reguladoras de los países miembros. Se redactan documentos de consenso técnico y científico en materia de seguridad, eficacia y calidad de MH, evitando la duplicación del esfuerzo regulador, creando las bases de un uso sostenible de recursos valiosos y resolviendo la falta de normativa en áreas importantes de la salud publica.

REGULACION TRASNACIONAL EN EUROPA

La Unión Europea, recientemente ampliada a 27 miembros, y un total de 470 millones de consumidores, provee un espacio altamente regulado para la armonización del mercado. La Agencia Europea del Medicamento (EMEA) que fue creada como organización reguladora trasnacional de la Unión en materia de medicamentos, ha desenvuelto su papel de manera tan exitosa que la OMS la ha tomado como modelo de sistema de gestión de información y la promueve como referencia en todos sus foros regionales (Lepakhin, 2004).

La regulación inexorable de todos y cada uno de los productos europeos ha llegado a los productos herbarios que, desde 2004, están en la cuenta atrás de su regulación obligatoria como Medicamentos Tradicionales Herbarios o a su degradación a la categoría de suplemento alimentario a partir de 2011. Para mas detalles léase el artículo escrito por Peschel (2007) en este mismo número. Cumplido este objetivo de regular la medicina herbaria “occidental”, Europa se ha embarcado en la creación de canales privilegiados con China y ASEAN para la futura integración de la MTC y otros productos del Sudeste Asiático en el mercado europeo (Ministry of Science and technology of RRPP China, Ministero Della Sanita de Italia, Directorate General for Research EU, 2007; ASEAN, 2007a, 2007b.

REGULACION GLOBAL: SITUACION ACTUAL

Existen algunos movimientos de carácter más o menos mundial que pretenden la coordinación de los entes reguladores de medicinas. Una de ellas es la International Conference of Drug Regulatory Authorities (ICDRA), que desde 1980 sostiene reuniones bianuales. Es una iniciativa de la OMS para proveer un foro único par a las autoridades reguladoras de todos sus estados miembros, determinando las prioridades de acción a nivel nacional e internacional de regulación de medicinas, vacunas, biomedicinas y medicamentos herbarios (WHO, 2007; Lepakhin, 2004).

Los objetivos de ICDRA son definir criterios y normas de calidad para medicinas herbales, alimentos funcionales y suplementos dietéticos entre todos los estados miembros y junto a la OMS, la cual continuara a desarrollar guías de calidad, seguridad y eficacia de MH y sus combinaciones. La OMS también pretende impulsar un programa de monitorización de uso y seguridad de MH, iniciativa que debe ser fortalecida e implementada pos los estados miembros. La OMS también seguirá proporcionando apoyos a estados miembros, especialmente en vías de desarrollo, para desarrollar programas de información sobre el adecuado uso de MH por parte del público. A nivel gubernamental, la OMS provee asesoramiento en la educación del personal sanitario. La ICDRA coordinara toda la información generada a través de estos programas. (WHO, 2007; Lepakhin, 2004)).

Otra iniciativa global de la OMS es la llamada Cooperación Internacional en materia de Reglamentación de los Medicamentos Herbarios (IRCH), cuyo objetivo principal es el de fomentar y facilitar el uso seguro de los medicamentos herbarios a nivel mundial, a través de iniciativas regionales, del intercambio de información y del diálogo (ICDRA 2006). Esta aun en su fase inicial y ahora se centra en la creación de una red de intercambio de información sobre aspectos técnicos de la regulación de MH mediante comunicación electrónica a diario entre los

"Information Focal Point" nominados por cada miembro del IRCH y la organización de reuniones anuales bajo el nombre de la "Global Strategy for Traditional Medicine", cuyo grupo de trabajo acordó desarrollar una segunda serie de monografías de Plantas medicinales en sus reuniones de Ottawa (Canadá) en 2005 (IRCH, 2005) y Beijing (China) en 2006, donde asistieron autoridades reguladoras de cada uno de los grupos de las seis regiones/sub-regiones de la OMS así como grupos de cooperación internacional incluyendo FHH, PANDRH, the European Herbal Medicines Committee, the ASEAN Product Working Group on Traditional Medicines and Health Supplements (TMHSPWG) y el parlamento Latino Americano (PARLATINO) (Zhang, 2006).

En contraposición a estos movimientos de globalización "populista" mediante foros y organizaciones cuya pertenencia esta abierta a todos los países, y dotados de organización interna flexible se sitúan los modelos "corporativos" de armonización global de medicinas, como la ICH. La opción corporativa esta caracterizada por una estructura altamente formal y definida, cuya pertenencia es restringida, que establece objetivos y fechas de entrega de resultados (Molzón, 2003).

La ICH es una organización internacional en la que participan países europeos, Japón y EEUU así como el Ministry of Health, Labour and Welfare de Japon (MHLW), la European Federation of Pharmaceutical Industries Associations (EFPIA), la Japan Pharmaceutical Manufacturers Association (JPMA), Food and Drud Administration (FDA) y la America's Pharmaceutical Research Companies (PhRMA) para el desarrollo de requerimientos técnicos homogéneos para productos medicinales. Aunque las normativas desarrolladas en este foro solo aplican a los países miembros, es evidente que el peso de los mismos en el mercado marcan las pautas a seguir a nivel global. Existe un Comité dedicado a MH dentro de esta organización, aunque no existen aun desarrollos tangibles.

LA AMENAZA BIOTERRORISTA COMO FUERZA REGULADORA

Hechos totalmente alíenos al mundo de las plantas medicinales han impulsado una regulación global *de facto* para las plantas medicinales. Los atentados del 11 de septiembre de 2001 dieron lugar a la aprobación del acta de bioterrorismo de la FDA (regulation 21 CFR Part 1, Subpart I), de acuerdo a la cual todos los productores de suplementos alimentarios (categoría que en EEUU corresponde a los MH) que quieran registrarse en esta agencia deben cumplir las GMP. China ha sido una de las mas afectadas debido al alto volumen de especialidades herbarias exportadas desde este país (Chan, 2003; FDA, 2003).

CONCLUSIONES

Se ha iniciado un movimiento a escala planetaria de globalización de los distintos sistemas de medicina tradicionales así como de homogenización del mercado de medicamentos herbales y plantas medicinales. El impulso inicial dado por los trabajos de la OMS y el ejemplo de la primera regulación trasnacional, en la forma de la Directiva de Medicinas Tradicionales Europeas, han sentado las bases documentales y legales para ayudar a una rápida implementación de medidas trasnacionales en otros continentes. Podemos pronosticar que en la próxima década la implementación de distintos consensos regionales sobre esta materia, siendo los más avanzados aquellos que se desarrollan dentro de espacios económicos comunes, como MERCOSUR o ASEAN. África ha comenzado por la creación de un marco estable a nivel continental para la medicina tradicional como paso previo a la regulación trasnacional. Tanto África como ASEAN se han marcado el 2010 para cumplir estas perspectivas. Si bien una regulación global tardara en conseguirse, diversos organismos ya han emprendido este camino en forma de encuentros regulares entre agencias reguladoras de todo el mundo.

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The Traditional Herbal Medicine Directive within the European regulatory framework for Herbal Products

[La Directiva Europea de Medicamentos Herbales Tradicionales en el contexto Europeo de Productos Herbales]

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Abstract

A series of new European guidelines specifically for herbal medicine has been generated over the last 10 years, which is embedded in the general harmonisation process of medicines regulation within the European Union. Although not generally welcomed, the need for quality and safety standards has been backed by a number of adverse events associated with herbal products often affecting several European member states simultaneously. Within this framework, the European Directive (2004/24/EC) for a simplified registration of traditional herbal medicinal products established a new harmonised way of marketing authorisation under consideration of national peculiarities. This paper gives an introduction to the current five regulatory pathways and the eligible guidance for herbal medicine in Europe.

Keywords: Traditional European Medicine, herbal medicine regulation, safety, quality.

Resumen

En el ultimo decenio se han generado una serie de guias europeas sobre medicamentos herbarios que se enmarcan en un proceso de armonizacion general del Mercado farmaceutico en la Union Europea. Aunque no siempre bien recibidas, la aparicion de efectos adversos ha veces afectando a varios paises miembros simultaneamente, han creado necesidad de reforzar las normas de seguridad y calidad A. Es en este contexto que aparece la Directiva Europea (2004/24/EC) para la registración simplificada de productos medicinales herbarios tradicionales ha establecido una nueva via de armonizacion del mercado considerando las peculiaridades nacionales existentes. Este articulo pretende introducir al lector en las cinco diferentes maneras de registro y la eligibilidad para los medicamentos herbarios en Europa.

Palabras clave: Medicinas Tradicinales Europeas, Medicamentos herbales, regulación,seguridad, calidad.

List of Abbreviations:
BfArM: Federal Institute for Drugs and Medical Devices (Germany)
CHMP: Committee for Human Medicinal Products
CP: Centralised Procedure
CTD: Common Technical Document
DCP: Decentralised Procedure
EC: European Commission
EMEA: European Medicines Agency
ESCOP: European Scientific Cooperative on Phytotherapy
HMP: Herbal Medicinal Product
HMPC: Committee for Herbal Medicinal Products
HMPWP: Herbal Medicinal Products Working Party
MA: Marketing Authorisation
MHRA: Medicines and Healthcare Products Regulatory Agency (UK)
MP: Medicinal Product
MRP Procedure of Mutual Recognition between Member States
Ph Eur Pharmacopoeia Europea
SPC Summary of Product Characteristics
THMP Traditional Herbal Medicinal Product
WEU Well Established Use
WHO World Health Organisation

1 THE CHALLENGE TO REGULATE HERBAL MEDICINAL PRODUCTS IN EUROPE

Herbal products for health purposes have been used traditionally in all European countries, most of them now member of the European Union with all legal consequences. In the past, the way of market access and legal handling is almost as heterogeneous as the botanical and ethnopharmacological patchwork of the plants behind these products. The herbal medicinal market in Europe is currently affected by substantial changes of the regulatory environment. Efforts are driven by the general intention to harmonise the regulation of medicinal products, food and other consumer goods at centralised European level. On the other side, authorities are particularly reacting to a changing European market and cases of adverse events linked to the consumption of herbal products. Safety issues arose both from well known HMPs registered or licensed for years in the EU (*Hypericum*, *Kava-Kava*) but also from imported products due to the increasing popularity of non-European traditional herbal medicine, mainly the Chinese one [Stickel et al. 2003, Singh 2005, Nortier & Vahherweghem 2002]. The first group is characterised by the increasing scientific knowledge about side effects/interactions, but also by the growing public awareness including the media and competitors from the synthetic drug market that herbal medicine is not in general harmless [Elvin-Lewis, 2005]. The second group of "imports" is accompanied by a series of new challenges which in this extent were not relevant for a more national "pure" European market so far. This refers to the increasing numbers of poor or wrong declarations and adulteration with heavy metals, other toxic plants or synthetic drugs [Ernst, 2002].

Both trends caused a series of adverse events, some of them with fatal outcomes. But also arose often exaggerated conclusions and warnings about the toxicity of HMP. Herbs and derived products can face a general condemnation, even when case reports are characterised by obvious overdosing, unclear sources, or doubtful products which than is compared 1:1 to the correct use of standardised products [Gruenwald et al. 2003]. However, in order to differentiate the good, the bad and the ugly, each consumer, manufacturer, regulator and journalist has to face some key issues, which differ from synthetic MP: the heterogeneity of the starting material itself (chemical composition, natural variability, diverse sources), the heterogeneity of plant preparations (plant part used, type of preparation, manufacturing process), and the lack of accurate quality/safety data for often non-standardised low price products. All three points require a careful analysis of any adverse event in particular when it comes to the transfer of data and some kind of "clan liability" for products, which are not comparable. Furthermore it can be stated that certain toxicity is well accepted for synthetic MP according to risk benefit assessments, whereas the "*generally regarded as safe"* paradigm and subsequent poor regulation level of HMP worldwide can cause certain overreaction.

Herbal medicinal products are classical borderline products and the term herbal medicinal product as such an umbrella term for a complex variety of products which have only in common to be of herbal origin and to be health related [Barnes 2003]. The very natural grey area between food and medicine, cosmetics and medicine etc. will always cause demarcation problems, even more when the very competitive food/cosmetic market tends to use health claims for marketing reasons. Understandably, small manufacturers of medicine try to avoid the considerable burden of medicinal law and customers prefer low price products if no risks are associated with them. Therefore, the priority of medication or nutrition/ cosmetic use, the duration and frequency of the application, and "natural or enriched" concentration of natural substances affecting physiological functions might be of decisive importance for product classification (see also Table 1). This interface is getting more complicated when the miscellaneous mixture of herbal products itself and all kind of combinations can cause the allocation of the same plant/product into various categories, not only by the intention of use but by the concentration and daily dose or only the type of package declaration on otherwise identical preparation.

Beyond this primary borderline a secondary one exists within the herbal medicinal products themselves. Traditional herbal medicinal products join now the well established use category and the full marketing authorisation and homeopathic medicinal products at European level. Thus, the manufacturer has often various options for which licensing process to go (Table 1).

The complexity of the matter multiplies when quality/safety standards shall apply for the entire European level. The heterogeneity of the European market (diverse cultures and traditions, import market, immigration), but also the heterogeneity of

the regulatory handling (National peculiarities, borderline to food and cosmetics) and subsequent diverse manufacturer and consumer patterns require balanced and cautious changes. The patchwork of regulatory tradition within the EU includes countries which traditionally deal with HP predominantly as medicinal product (Germany, Austria, Denmark), as "traditional" medicinal product (France, Spain, Sweden) or exempted from medicine law mostly registered as food (UK, Benelux, Portugal). Usually all member states accept various categories for herbal medicine from the legal point of view and few efforts are made to clarify grey areas and to suit action to the word [Benzi & Ceci 1997].

2 EUROPEAN REGULATORY BODIES AND LISTING/MONOGRAPH SYSTEMS

The European Union is tackling these uncertainties of the herbal sector for a decade now and has established a decent framework of guidelines which at least in part will harmonise the European market (Table 2). However, national peculiarities will remain and a comparable degree as for synthetic products with single chemical entities will probably never be reached. The new traditional herbal medicine directive 2004/24/EC (embedded in 2001/83/EC art. 16) plays a central role amending the well established use category (2001/83/EC art. 10a – 2003/63/EC) as an alternative between food (almost no health claims possible) and full marketing authorisation including efficacy (2001/83/EC Art. 8). Beside the upgrading of the EMEA based herbal medicinal products working party (HMPWP) to the committee level (HMPC) with the guideline EMEA/HMPC/139800/2004, herbal specific guidelines of different binding level are focussing now on four key areas: demarcation/classification (e.g. directive 2004/24/EC), quality (e.g. guideline CPMP/QWP/2819), safety (e. g. public statement 138139/2005) and on standardisation/declaration problems (e.g. EMEA/HMPC/CHMP/CVMP/287539/2005) (for an overview see Table 2). This package has to be understood as amendment to general medicine law focusing on the peculiarities of herbal products and providing either detailed extension or useful simplification considering their specific status. That means for instance, if the full quality part 2.1 of the common technical document is required, it includes also the GMP conform production process – a specific challenge (and sometimes not manageable hurdle) for small manufacturers. On the other hand,, the time and effort of quality control, stability tests and declaration of multicompound mixtures can by far exceed single chemical entity products. This requires expertise and sensitivity at commissions/authorities to balance well between safety and appropriate expenditure.

Before the European Commission, and the EMEA/HMPC became the key players for the regulation of the herbal market, there has been other organisations facing the acclamation of diverse national situations. This refers mainly to the European Directorate for the Quality of Medicines (EDQM) with the Commission of the European Pharmacopoeia (Ph Eur) in Strasbourg and the European Scientific Cooperative on Phytotherapy (ESCOP, founded 1989). The EDQM includes 36 European Member States and 20 observers such as the American FDA and the WHO. Its role is to harmonise the quality standards for use by healthcare professionals. The Ph Eur is the only official pharmacopoeia in Europe to be used for international trade and it is mandatory in European marketing authorisation dossiers in 36 member states. The group of experts from the Ph Eur is proposed by all national authorities and appointed by the Ph Eur commission. The ESCOP was a voluntary organisation in order to extent European HMP quality standards to the scientifically approved effective and safe use. The first national data based approach of major dimension was the German so called Commission E within the Federal Health Institute. This means, on the basis of national monographs there was already the attempt to create standards in terms of quality (EDQM), safety/efficacy (ESCOP) for the most common plants at the European level. These monographs usually represent the state of the art and provide the basis for well established use (WEU) applications (for a comparison see Table 3). Subsequently ESCOP and Ph Eur monographs are now the starting point for the WEU and THMP monographs established successively by the HMPC. This development is of course discussed controversially either criticising double standards as well as fearing simplification to a European gold standard without consideration of traditionally/scientifically justified product diversity. Likewise, other herbal medicine specific topics have not only there national, but also international anticipators. The Good Agricultural Practice guideline for herbal starting materials (246816/2005) for instance has been built on guidelines from the

EUROPAM (The European Herb Growers Association, first version 1998), and the WWF Traffic network, starting together with other organisations 1993 with the Guidelines on the Conservation of Medicinal Plants.

The division of legal, administrative and enforcement tasks and responsibilities between the European commission (Enterprise and Industry Directorate General, F/2 Pharmaceuticals) in Brussels, the EMEA in London (HMPC, quality group, CHMP, etc) and national authorities of the member states (e.g. MHRA in UK, BfArM in Germany, AGEMED in Spain) is not always as transparent for non-insiders as it should be. Furthermore different types of European law of either guiding ("soft law") or directly binding character as well as the differentiation between direct EU regulations, EU directives to be implemented by the member states into national law, and pure national law will cause some confusion for any HMP manufacturer. However, by now and in the near future, the herbal sector practically will mainly deal with national authorities as either for a national MA or for the MRP procedure. The adoption and legibility of European law is task of the national regulating authority and their advice is fundamental for the final decisions. A good communication basis with the national authority for an expertise driven exchange of opinions is the key for pragmatic solutions in this virgin soil of pan-European HMP regulation. There are only a few experiences yet with the new regulations; hence their practicability has to be shown in the future. There are only 8 products in three member states registered under the new traditional use legislation so far. 79 applications in 12 MS are reported [Woodfield 2007]. Both statistics reflect the difficulties in the implementation. Already now, key issues crystallise such as the community monograph/listing process, the demarcation between WEU and TU, the different law interpretation of national authorities, the proof of traditional use, the flexibility in product adaptation in terms of strength and posology ("comparable" preparations, "minor" changes, "essentially similar", modern dosage forms etc.), the handling of combination products, but also aspiration to protect the partially strong herbalist and food supplement sector established in some MS [Roether 2006, Krisper 2007].

3. HMP WITH FULL MARKETING AUTHORISATION AND BIBLIOGRAPHIC APPLICATION (WEU)

According to 2001/83/EC as for any other medicinal product HMP MA can be obtained under central procedure (CP), decentralised procedure (DCP) or mutual recognition of national MA (MRP). However, many herbal medicinal products are still licensed on a national basis due to the differences in national practices with respect to such products. HMP for which sufficient evidence is available to support the quality, safety and efficacy of the product must apply for a full MA. Applications with full supporting data, as usual for so called new chemical entities (NCE), are rare; more common is to go for the "well-established use" provision of a bibliographic application according to Article 10 of Directive 2001/83/EC on the basis of published literature (see alsoTable 1). In the broadest sense are these generic applications, whereby the comparator referred to is not an already established product after data protection time but a monograph and/or other accepted scientific core-data. This means also, that those products will usually not be accepted as THMP, as efficacy/safety data are available and have not to be replaced by the proof of traditional use. But differences of the product and authority practice in the member states will cause doubling e.g. a *Harpagophytum* product is licensed as traditional medicine in UK whereas *Harpagophytum* products are not "traditional" but "well established" for German authorities due to sufficient safety and efficacy data. By now, only one HMP is listed for the CP (a *Boswellia* extract), no experiences exist for the DCP yet and less than 20 products have successfully received MA under MRP.

"Core-data" (previously called core-SPCs) as outlined in section before, originate from the monographs produced by WHO, ESCOP, and are increasingly replaced by community herbal monographs elaborated by the HMPC according to standard procedures (107436/2005 and 182352/2005). These core-data can facilitate the authorisation process but are not legally binding. Whenever such monographs have been adopted the registration holder will be required to amend the registration dossier to comply with the new monograph. Only when no such monographs have been established, other appropriate monographs, publications or data may be referred to. The process of monograph and list establishment can be followed

Table 1. General overview on EU regulation types for health related herbal products

Category	Subcategory	Legal basis	Main characteristics
HMP with MA	Full dossier new MA, (DCP, MRP, CP)	§8(3) directive 2001/83/EC	full CTD including safety/efficacy data
	Bibliographic application (well established use), (MRP, DCP)	§10a directive 2001/83/EC WEU defined by Annex 1 of 2001/83/EC amended by 2003/63/EC	no individual but bibliographic – safety/efficacy data (mixed applications possible)
HMP with simplified registration	Registration as Traditional Herbal Medicinal Product (THMP)	§ 16a directive 2001/83/EC, amended by 2004/24/EC	full quality part, safety replaced by expert statement, efficacy replaced by traditional use (30/15 years)
	Homoeopathic MP Anthoposophic MP (treated legally as homoeopathic according directive 92/73/EEC)	§ 14-15 directive 2001/83/EC	simplified registration, no individual safety/efficacy data
HP outside medicine legislation	Food supplements Cosmetic products Consumer goods	e.g. 178/2002/EC for demarcation foodstuffs-MP, 2002/46/EC for food supplements; Cosmetic Directive 76/768/EEC + 93/35/EEC	mainly notification only

on the EMEA website and also pharmaceutical manufacturers can comment the drafts before adoption (http://www.emea.europa.eu/htms/human/hmpc/mpclist.htm).

One of the main actions of the HMPC is to facilitate the use of the mutual recognition procedure for herbal medicinal products. This means that in contrast to the THMP (see section below), the HMPC has only supporting functions for the fully responsible CHMP in case of full dossier and WEU applications. This is being done in part by updating the guidance documents relating to bibliographical applications and by promoting the core-data documents as a means of facilitating the assessment of safety and efficacy.Considering the still missing experience with CP and DCP, here only some key points for a bibliographic application via MRP are outlined: In general the format for an application for MA must be based on the Common Technical Document (CTD), consisting of 5 modules, whereby the results of non-clinical tests and clinical trials (modules 4 and 5) are replaced by references to published scientific literature. The content of modules 1 (includes SPC), 2 (administrative data) and 3 (quality) is equivalent to any other MP as specified in Directive 2001/83/EC, including some legally binding specific details in Annex 1. Further "soft law" guidance is given in Chapter 1 Volume 2A and 2C of the Notice to Applicants and in various HMPWG/HMPC guidelines. These are for instance: guidelines addressing quality in general (CPMP/QWP/2819/00); specifications and test procedures (CPMP/QWP/2820/00) and biopharmaceutical characterisation (EMEA/HMPWP/344/03). During the consolidation period of HMPC monographs/lists, the Ph Eur monographs provide still eligible quality standards and it is also possible to obtain EDQM certification. Manufacturers meeting the criteria set out in this list/monographs will not have to demonstrate individually compliance with the criteria for WEU and safety, but will still have to meet the normal requirements regarding quality. This means first of all that the principles and guidelines of GMP apply. Annex 7 of the GMP guide provides specific guidance for herbal medicinal products (EC Eudralex Volume 4). Annex 18 of the GMP guide relating to requirements for pharmaceutical active ingredients should also be considered, while factors concerned with the primary production and processing of the herbal drug is covered by the already mentioned good agricultural and collection practice guideline EMEA/HMPC/246816/2005.

Table 2. Herbal medicine specific guidelines within the EU regulation according to the main areas classification, quality, safety/ pharmacovigilance and efficacy

Classification/demarcation/standardisation/declaration
DIRECTIVE 2004/24/EC of the European parliament and of the Council of 31 March 2004 amending … Directive 2001/83/EC on the Community code relating to medicinal products for human use
EMEA/HMPC/261344/2005 Concept paper on CTD for traditional herbal medicinal products
EMEA/HMPC/CHMP/CVMP/287539/2005 Guideline on Declaration of Herbal Substances and Herbal Preparations in Herbal Medicinal Products/Traditional Herbal Medicinal Products in the SPC3
EMEA/HMPC/107436/2005 Template for a community herbal monograph (Rev. 2)
EMEA/HMPC/182320/2005 Procedure for the preparation of community monographs for traditional herbal medicinal products
EMEA/HMPC/182352/2005 Procedure for the preparation of community monographs for herbal medicinal products with well established medicinal use
Quality
CPMP/QWP/2819/00 Guideline on the Quality of Herbal Medicinal products/Traditional Herbal Medicinal Products
CPMP/QWP/2820/00 Guideline on Specifications: Test procedures and acceptance criteria for Herbal Substances, Herbal Preparations and Herbal Medicinal Products/Traditional Medicinal Products
EMEA/HMPC/125562/06 Reflection Paper on the use of Fumigants
EMEA/HMPC/CHMP/CVMP/58222/06 Concept Paper on Quality of Combination Herbal Medicinal Products/Traditional Herbal Medicinal Products
EMEA/HMPC/246816/2005 Guideline on Good Agricultural and Collection Practice (GACP) for starting materials on herbal origin
Safety + Pharmacovigilance
EMEA/HMPC/104613/2005 Guideline on the assessment of clinical safety and efficacy in the preparation of monographs/lists for traditional herbal medicinal products/substances/preparations
EMEA/HMPC/317913/06 Reflection Paper on the risks associated with furocoumarins contained in preparations of *Angelica archangelica* L.
EMEA/HMPC/413271/06 Concept paper on the development of a guideline on the assessment of genotoxic constituents in herbal substances/preparations
EMEA/HMPC/138139/2005 Public statement on the allergenic potency of herbal medicinal products containing Soya or Peanut Protein
EMEA/HMPC/138309/2005 Public statement on Chamomilla containing herbal medicinal products
EMEA/HMPC/32116/05 Guideline on Non-Clinical Documentation for Herbal Medicinal Products in Applications for Marketing Authorisation (Bibliographical and Mixed Applications) and in Applications for Simplified Registration
EMEA/HMPC/246736/05 Public Statement on "CPMP List of Herbal Drugs with serious risks, dated 1992"
EMEA/269259/06 EMEA Public Statement on herbal medicinal products containing *Cimicifugae racemosae rhizoma* (Black cohosh, root)
EMEA/HMPC/269258/06 *rev 1* Assessment of case reports connected to herbal medicinal products containing *Cimicifugae racemosae rhizoma* (Black Cohosh, root)
EMEA/HMPC/139215/05 Public Statement on the use of herbal medicinal products containing asarone
EMEA/HMPC/138381/05 Public Statement on the risks associated with the use of herbal products containing Aristolochia species
EMEA/HMPC/138386/05 Public Statement on the use of herbal medicinal products containing pulegone and menthofuran
EMEA/HMPC/138379/05 Public Statement on Capsicum /capsaicin containing herbal medicinal products
EMEA/HMPC/137212/05 Public Statement on the use of herbal medicinal products containing estragole
EMEA/HMPC/138363/05 Public Statement on the use of herbal medicinal products containing methyleugenol
Efficacy
EMEA/HMPC/104613/05 Guideline on the assessment of clinical safety and efficacy in the preparation of community herbal monographs for well-established and of community herbal monographs/entries to the community list for traditional herbal medicinal products/substances/preparations
EMEA/HMPC/166326/05 Guideline on the Clinical Assessment of fixed Combinations of Herbal Substances /Herbal Preparations

4. TRADITIONAL HERBAL MEDICINAL PRODUCTS

The so called "Traditional Use Directive" 2004/24/EC had to be implemented by member states (MS) by 30/10/2005. This has been realised by most MS with some delay (except Check Republic, Ireland, Netherlands, and Norway as associated MS). However, difficulties in the transition and establishment of enforcement rules still remain in 15 MS [EFPIA Draft Document: Status of Implementation of the European Union Pharmaceutical Legislation at Member State Level, 16/05/2007]. A transitional period is given for traditional herbal medicinal products which were already on the market on the 30/04/2004 (date of entry into force of Directive 2004/24/EC). This allows sufficient time for regulators/manufacturers to adapt to the new requirements and to accumulate evidence of usage in the EU of existing products. By 2011 all old/new herbal medicinal products will have to licensed/registered in order to stay on the market. 2004/24/EC can apply when applicants provide evidence relating to traditional use, quality and safety in accordance with the requirements detailed in Articles 16b and 16c 2001/83/EC (Table 4). This allows a derogation from the standard efficacy requirements when justified by the product's safety profile, i.e. safe traditional use for a minimum of 30 years thereof 15 within the EU. To prove this, bibliographic or expert evidence will be required either for the product concerned or "a corresponding product". Whereas efficacy data are completely replaced by the traditional use, a bibliographic review of safety data together with an expert report will be required as it is usual for the WEU (see section above). In critical products it can happen that the authority request own data necessary for accessing the safety of the product. This may apply specifically in response to actual developments or recent safety issues, as happened with the interaction potential of various HP.

When relating to a corresponding („or comparable") product, active ingredients, the intended purpose, the route of administration have to be the same or similar, and equivalent strength and posology are expected as well. The law allows only that the number/quantity of ingredients may have been reduced during the qualifying period of traditional use. The practical interpretation of the legal terms "comparable", "similar", "equivalent" and the usefulness of combinations and removal of single ingredients will cause some discussion and vary possibly between the regulators of different MS. The directive implies further restrictions for traditional-use registrations as the intention for use without the intervention of a medical practitioner, whether for diagnostic purposes, prescription or monitoring of treatment. Any intravenous and intramuscular administrations are excluded and THMP restricted to herbal medicines that are taken orally, or are for external use or inhalation.

The borderline to food is addressed when stating: "Registration of traditional herbal medicinal products combined with vitamins or minerals may be possible, where there is evidence of safety and where the action of the nutrient is ancillary to that of the herbal active ingredients." Also the borderline to WEU and homoeopathic products is explicitly mentioned: "Herbal medicinal products which can be given a marketing authorisation on the basis of supporting safety and efficacy data (e.g., using published papers) will not be eligible for the simplified procedure. Likewise homeopathic medicines will be excluded."

The format and content of application for a traditional use registration application will be based on the Common Technical Dossier (CTD). Specific requirements for herbal products will apply accordingly to full MA applications, which includes the use of core data by positive lists and monographs. Likewise to WEU products the normal quality requirements applicable to a licensed medicinal product will apply. Thus compliance with GMP (including Directive 2003/94/EC) will be required. GMP will also apply to herb active ingredients used as active substances. There will be a requirement to hold a Manufacturer's Licence and/or Wholesale Dealers Licence as appropriate. Release of manufactured/ imported batches will require certification by a qualified person. In addition to the requirements of Articles 16b and 16c many of the other provisions of Directive 2001/83/EC will apply for THMP. These are listed in Article 16(g) and include aspects such as pharmacovigilance, labelling (including Braille) and user testing of patient information leaflets.

5. REGISTRATION OF HOMOEOPATHIC HMP

Homoeopathic remedies inclusive anthroposophic remedies are the other exemption from normal MA procedures as outlined in Article 13-16 Directive

Table 3. Relevant monograph systems as basis for bibliographic applications of THMP and HMP (WEU and mixed applications). The total number of plant related monographs includes different monographs of different substances (e.g. herb, root), preparations (fruit, extract, dry extract) of the same species as well as general monographs (e.g. herbal extracts)

Organisation	Included species	Total number of monographs	Comment
Commission E	190	380	Elaborated in the 90s by an Expert committee formed by the German government within the Federal Health Institute (BGA)
ESCOP	73	80	Following the work of the Commission E the ESCOP Scientific Committee (initially funded by the EC) is reviewing the therapeutic uses of HMP, monographs are updated/recognized by the EMEA
WHO	54	58	Compiled by 120 experts in more than 50 countries and published in 2 volumes (1999, 2002), rather secondary status in Europe
Ph Eur	126	>180	Quality only. Compiled by expert committee within the EDQM. Mandatory status in Directives 2001/83/EC, 2003/63/EC, and 2001/82/EC as am. The only official pharmacopoeia quality standard in Europe to be used for international trade. Constantly updated; last June 2007
EMEA/HMPC WEU	8 (3 drafts)	9 (3 drafts)	HMPC experts consultation based on Ph. Eur and ESCOP monographs drafts are released for public consultation on the web for 3 months. Further in preparation: 8 monographs where the draft is under discussion, 33 monographs with assigned rapporteur (June 2007)
EMEA/HMPC TU	2 (10 drafts)	2 (12 drafts)	

Table 4: Article 16a (1) (2001/83) criteria for the simplified procedure as traditional medicine, where the efficacy is supposed to be plausible based on long-standing use and experience and some examples for difficulties in law interpretation.

Criteria	Examples for interpretation	
	Includes:	**Excludes:**
• indications exclusively appropriate to THMP	• design for self medication e.g. with cautios health claims such as *"symptomatic relief of... "*	• diagnostic purposes, required prescription, monitoring treatment, required supervision of a medical practitioner, serious diseases e.g. HTV
• specified strength and posology	• aqueous extract instead of tea • exact/comparable concentration • same or reduced number of ingredients in combinations	• tablets instead of tincture • not comparable concentration • replacement of ingredients in combinations
• for oral, external or inhalation use only	• tablets, ointments, tinctures etc. • comparable non-traditional modern dosage forms such as sprays	• intravenous, intramuscular • non-comparable non-traditional modern dosage forms such as sprays
• sufficient data on the traditional use • minimum 30 years traditional use, including at least 15 within the EU	• case by case • geogr. non-European but politically European areas such as French Guyana • all new EU member states	• case by case • when less than 30/15 years (but other conditions can apply = HMPC but not National decision)
• prove not to be harmful in the specified conditions	• in general given with traditional use and expert statement	• new data situation indicating risks • genotoxicity/cancerogenicity not excluded by traditional use

Cuadro 1: recommended websites for further information on European regulatory affaires.

http://www.mhra.gov.uk	http://www.hma.eu	http://www.ifpma.org
http://www.agemed.es	http://www.emea.eu.int	http://www.ich.org
http://www.bfarm.de	http://www.who.int	http://www.phrma.org
http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/	http://www.efpia.org	http://www.escop.com

2001/83/EC. A simplified registration procedure for those products placed on the market without therapeutic indications is specifically envisaged by Article 14(1) of Directive 2001/83/EC as amended.

A homoeopathic MP is according to Directive 2004/27/EC (amendment to 2001/83/EC) newly defined as: "Any medicinal product prepared from substances called homeopathic stocks in accordance with a homeopathic manufacturing procedure described by the European Pharmacopoeia or, in the absence thereof, by the pharmacopoeias currently used officially in the MS. A homeopathic medicinal product may contain a number of principles." These may include non-herbal starting materials, which are not yet considered for the traditional use directive. The homeopathic registration scheme is also a simplified regulatory procedure, whereby products are assessed for their quality and safety. The simplified scheme does not allow indications or therapeutic claims. Thus, efficacy data are not required. Often registration under the scheme is compulsory only in respect of products new to national markets. In order to qualify for registration under the simplified procedure, the products must be for oral or external use. This includes all methods of administration with the exception of injections. In general homoeopathic MP must be sufficiently dilute to guarantee their safety.

Of course companies also have the option of obtaining a full marketing authorisation for homoeopathic remedies, provided that the regulatory requirements for safety and efficacy can be satisfied. When a "traditionally used" homoeopathic stock of plant origin (practically ethanolic extract or tincture) without further dilution is used, in some cases the manufacturer may have the decision between simplified regulation under the traditional use or the homoeopathic category, which in general are exempted to each other (see above). In both cases, no efficacy data have to accompany quality (including shelf life tests) and safety data. Differences in labelling and marketing (no indication and health claims for homoeopathic products), existing monographs and listing and the data situation to support the WEU will contribute considerably to the manufacturers case by case choice of the appropriate regulatory strategy.

Comparable to allopathic herbal medicine the regulation of homeopathic products is predominantly characterized by National traditions and rules. In UK for instances the Advisory Board on the Registration of Homeopathic Products (ABRHP) gives advice in respect of which a certificate of registration could be granted. However, the European harmonisation process is on track and various European organisations will find each other under the umbrella of the Homeopathic Medicinal Product Working Group (HMPWG), which informal meetings first started in 1999. The participants of HMPWG are assessors and regulatory experts from the National Competent Authorities, as well as representatives from the EC, Ph Eur, EMEA and WHO. The group was formalised by the Heads of Medicines Agencies (HMA) in 2004. The HMPWG is a forum of exchange of regulatory and scientific expertise as well as elaboration and provision of guidance to assessors and applicants and expertise and advice on request regarding procedural, regulatory and scientific issues arising from the MRP/DCP. It was started because there was a clear need for a European solution for the regulation of homeopathic MP due to the particular characteristics of this therapeutic system.

6. HERBAL PRODUCTS OUTSIDE MEDICINE LEGISLATION

The traditional use directive is most controversially discussed in European countries were the majority of HP were classified as food supplements, which facilitated market access without provision of detailed quality and safety data. Herbal remedies equally to minerals or vitamins have a classical "dual-use" – character, where nutrition/diet purposes are paralleled by health promoting/ therapeutic purposes. The classification a herbal product in the borderline is still dominantly national decision according to case by case studies based on law and tradition. But similarly to the Traditional Use Directive, the market of the single member states will be influenced by the pan-European food legislation in the future. The "general opinion" will consider the possible risk, the pharmacological characteristic due to current scientific knowledge, the degree to which the consumer is familiar with the product and the way in which the product is used. For many manufacturers of herbal products, it is getting more and more important to deal with the legal differentiation between medicine and food (respective cosmetics) which includes questions like:

- Which constituents are legal in food or cosmetics?
- Do they have any phamacological effect?
- Are there concentration limits?

- Which effects has the demarcation on advertisement, labelling and marketing?
- Is there already binding harmonised European law or are national niches still feasible?
- Which nutrition declarations have to be stated on package and leaflet?
- How to deal with health claims?

Step by step the EU will also harmonise the food law in terms of food supplements and their safety. A first definition of foodstuffs has been introduced with regulation 178/2002/EC for a harmonised demarcation between foodstuffs and medicinal products. Directive 2002/46/EC contains a definition for food supplements for the first time. Primarily there were no maximum/minimum levels for nutrients and/or substances with nutritional effect; which are important for drawing the borderline between food supplements and medicinal products. Furthermore, the directive covers only vitamins and minerals. In the near future, however, the directive could substantially limit the potency of nutrients in such products by reducing maximum permitted levels. And it may be applied to other nutrient groups such as fatty acids, amino acids, fibre, and plant extracts. It became fully implemented on August 2005, but further demarcation activities are also expected by EFSA (European Food Safety Authority), EMEA and the EC. A helpful overview on current European food legislation in terms of herbal products is given by Gulati & Ottaway (2006).

7 CONCLUSIONS

The manufacturer of a herbal medicinal product has now five main regulatory pathways for marketing in Europe. Within medicine law a full application, a well established use application or simplified registration as either traditional herbal medicinal product or as homoeopathic medicinal product are possible. The food supplements pathway will remain, but is likely to be further restricted. At least until 2011 old national regulatory pathways will linger. In general, the national procedure dominates clearly, however the number of European procedures in particular the mutual recognition (MRP) is expected to increase also for HP as soon as advantages for marketing in various member states is less inhibited by uncertainties of the new administrative trail. The directive 2004/24/EC for THMP is put to test in all member states and the solution of practical issues specifically associated with the transfer from old to new registrations a challenge to all national regulatory bodies and the EMEA/HMPC. A market clarification and increased safety level can be expected, however manufacturer and product diversity may be diminished.

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The Impact of the European Traditional Use Directive on the Herbal Product Markets in the United Kingdom, Germany and Spain

[El impacto de la Directiva Europea de Uso Tradicional en los mercados nacionales del Reino Unido, Alemania y España]

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Abstract

Herbal products have been regulated in different European member states either predominantly as medicinal product, as "traditional" medicinal product, registered as food or remained unregulated. With the European Directive (2004/24/EC) for a simplified registration of traditional products a new era of centralised medicinal product regulation has started also for manufacturers of herbal medicine. The regulatory impact on the industry will vary between European member states according to the respective starting point. It is likely to be larger in countries, where much of the industry has been operating in a rather unregulated market. In other countries, manufacturers are better prepared, because they had already to meet high quality standards, GMP requirements, or pharmacovigilance procedures. This paper summarises the current situation in three European member states with different history of herbal medicinal product regulation. The examples of UK, Spain and Germany demonstrate the challenges of regulation and harmonisation processes for herbal products which may be relevant also for Latin American countries in the future.

Keywords: Traditional European Medicine, herbal medicine regulation, Spain, UK, Germany.

Resumen

Los productos herbales han sido regulados en Europa de manera diferente, ya sea como producto medicinal, como "producto herbal tradicional", como suplemento alimentario o incluso dejados en un ambiente desregulado. Con la nueva Directiva Europea (2004/24/EC) para el registro simplificado de productos tradicionales ha empezado una nueva era de regulación de productos medicinales para los productores de medicinas herbales. El impacto de esta regulación en la industria variara entre los distintos estados europeos de acuerdo a sus respectivos puntos de partida en lo que a regulación nacional refiere. El impacto será posiblemente mayor en países donde la industria ha venido operando en un mercado más o menos desregulado. En otros países, los productores estan mejor preparados ya que venían largo tiempo obligados a cumplir normas de calidad elevadas incluyendo GMPs, farmacovigilancia o ensayos de estabilidad. Este artículo resume la situación actual de tres miembros de la Unión Europea con diferentes historias de procedimientos para la regulación y armonización de los productos herbales. Los ejemplos de España, Reino Unido y Alemania pueden ser relevantes para los países Latinoamericanos en el futuro.

Palabras clave: Medicinas Tradicinales Europeas, regulación de medicamentos herbales, España, Reino Unido, Alemania.

List of Abbreviations:

AGEMED	Agencia Española de Medicamentos y Productos Sanitarios (Spain)
EC	European Commission
HMP	Herbal Medicinal Product(s)
MA	Marketing Authorisation
MHRA	Medicines and Healthcare Products Regulatory Agency (UK)
MP	Medicinal Product(s)
THMP	Traditional Herbal Medicinal Product
WEU	Well Established Use

Websites used:

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http://www.bfarm.de
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http://www.hma.eu/
http://www.emea.eu.int
http://www.efsa.europa.eu
http://europa.eu/rapid/pressReleasesAction.do?reference=IP/07/403&format=HTML&aged=1&language=EN&guiLanguage=en

1 FROM AN UNREGULATED TO A REGULATED ENVIRONMENT – THE NEW CHALLENGE IN UK

Before implementation of the European Traditional Use Directive 2004/24/EC herbal products (HP) reached the UK market usually by three different routes: (1) as a fully licensed medicine, (2) as from a full licence exempted herbal remedy (so called section 12(2) exempts), or (3) as food supplement. (1) A marketing authorisation (MA) can be obtained under the Medicines for Human Use Regulations 1994 (SI 3144/1994) which largely transposed Directive 2001/83/EC into UK law. Under the Regulations most industrially produced MP that are placed on the market are required to be authorised demonstrating standards of quality, safety and efficacy. This full MA pathway including simplified bibliographic applications was practically irrelevant for HP.

(2) Section 12(2) of the Medicines Act 1968 (and regulation 1(3) of the 1994 Regulations) exempted herbal remedies that are not required to have a MA providing the remedy meets various conditions. Certain ingredients are prohibited or restricted, but otherwise there are no specific requirements as to safety, quality or efficacy. No written claims are permitted and there is no specific requirement in terms of consumer information and safe usage. The original idea was to facilitate HMP market access for herbal practitioners to make up herbal remedies without license on the premises from which they are supplied and to prescribe such remedies for an individual patient following a one-to-one consultation. Unfortunately this pathway has converted over the years into an easy market access also for industrially produced remedies (tablets, capsules etc.) in large scale.

(3) HP were often licensed as food supplement, which was uncomplicated “if the safe food use can be demonstrated for a herb”. It also allowed health maintenance claims, but no claims to treat, cure, or prevent a clinical condition. This health maintenance claim must be substantiated, if requested by Trading Standard Officers or the Advertising Standards Authority. A typical health claim is: “May help to maintain a healthy digestion”. However, neither demonstration of safe use nor the rational for health claims required pre-marketing activity by manufacturers. Some herbs were excluded if they are defined by the MHRA as “medicinal by function” such as *Hypericum*, *Echinacea*, *Valeriana* or *Cimicifuga*.

Because of missing quality standards and a lacking pharmacovigilance system, the categories (2) and (3) are the predestined trouble maker and responsible for major safety concerns. Colonial history and ongoing multiple immigration formed a market particularly vulnerable to “non-regulation”. The extensive international trade in unlicensed HP lead to various cases of substitution, contamination or adulteration, e.g. with undeclared prescription-only-drugs, poisons, or mislabelling. For example, in December 2004 the MHRA confiscated a consignment of 90,000 tablets containing a toxic ingredient, and in 2003 the MHRA found that a product containing 11.7% mercury by weight was available in 35 traditional Chinese medicine outlets. But not only risk to public health and public confidence, but also a risk to responsible businesses was stated by authorities: Manufacturers working under high quality standards have complained to the MHRA that they are undercut on price by those who formulate their products with low grade ingredients inadequately tested in terms of identity and purity (MHRA website; Anderson, 2007).Directive 2004/24/EC has been fully implemented by the British authorities and provides a new fourth category, by now mostly as transitional protection for products on the market before 30/04/2004. Already 5 products have been newly licensed under this category so far. However, many of the old Section 12(2) products will automatically fall under the traditional use category and reap the benefit of the long transitional period until 30/04/2011. By then, all THMP requirements have to be fulfilled otherwise the product has to be withdrawn from the market.

The extraordinary new requirements for the British food industry lead to a costs and benefit calculation by the MHRA. Several tens thousands of pounds are the additional costs associated with registering a product under the Directive as compared with the cost for an unlicensed herbal remedy placed on the largely unregulated market. This will vary according to the nature of the product and the circumstances of the individual company. Size may be relevant, for example, micro and small companies may be insufficiently equipped to carry out certain activities in-house and may need to buy in help. On the other hand, a medium sized or larger company that wishes to enter a number of European markets may well decide it is worth having state of the art dossiers and quality controls in order to minimise the

risk of delay arising from queries from the various regulatory authorities. If by 2011 around 500 products had been registered incurring various costs relating to registration at an average of £40,000 per registration, and if about 50% of the registrations related to UK companies, this would represent a cost to UK companies of about £10m spread over 6 years for bringing these products into regulation. This does not include some additional expenditure, notably in premises or equipment improvement, that some companies have recognised were needed in the interests of good standards (Anderson, 2007; Barnes, 2003; Helliwell, 2007; Mills, 2006; Woodfield, 2007, MHRA website)

2 NEW BORDERLINES – THE DEVELOPMENT IN GERMANY

Compared to the UK, the new European directive is of minor impact for regulators, customers and manufacturers in Germany because of four reasons: (1) HP with health claims have been traditionally treated as MP with similar quality and safety standards, (2) several monographs originating from the commission E of the former BGA (Federal Health Authority) facilitated already a "well established use" bibliographic application before ESCOP or WHO provided similar core-data, (3) a comparable paragraph for traditional use remedies has been created with the 5th amendment of German drug law (5. AMG-Novelle, 1994) after a long cleaning process of the pharmaceutical market, and (4) HMP were produced by small and medium pharmaceutical enterprises, which were working under pharma-specific production/documentation standards including control/inspection by regional, federal and international authorities.

The acceptance of traditional use as prove for quality and safety (point 3) is a transitional regulation only, caused by major delays in the revalidation of all German products on the market (§105 AMG together with §109a). Traditional MP, which were on the market before 1978, got a provisional MA until the post-marketing procedure has been completed. New products couldn't get the "traditional status", even if they were traditionally used. This refers not only to herbal MP, but also to any other "traditional" remedies. Because of its specific history Germany implemented as the first MS the Directive

Table 1. General overview on types of applications and market size for HMP in Germany (BfArM 2005)

Full Marketing authorisation procedure according §§ 21,22 AMG	Requirements as for all non herbal MP according § 22 ff. and AM-Pruef-RL. (Annex I RL 2001/83) Mostly based on well established use according monographs of the former commission E	In total 4551 herbal, traditional, homeopathic or anthroposopic medicinal products are licensed (Dec 2005)
Registration as Traditionally used according §109a AMG (implementation of 2004/24/EC)	Simplified procedure developed for a transitional period due to German retarded revalidation procedure in accordance with § 105 AMG in conjunction with § 109a AMG, valid for traditional MP which were on the market before 1978 (not for herbals only!),	1050 traditional medicinal products with completed post-marketing approval procedure are available on the German market(Dec 2005)
Registration as Traditionally used according §39a AMG	As Implementation of 2004/24/EC recent amendment to the 14th Version of the German drug law (AMG)	5 (April 2007)
Registration as homoeopathic product according §38-39 AMG	Simplified registration procedure already established, only slightly changed according European guidelines	3730 homeopathic medicinal products are registered (Dec 2005)
Notification under food or cosmetic law	LMBG, § 5 of NemV	No statistics available

2004/24/EC into national law (§ 39a – 39d AMG), which applies since September 2005. Now, traditional remedies have access to the market as "new products", if they are comparable to preparations which fulfil 30 years traditional use (15 years thereof in Europe). This European traditional HMP will replace in the long term the above mentioned transitional regulation of §105 in combination with §109a for "national traditional MP". By now , 2004/24/EC and 39a AMG refer to herbal products only, but in future the extension to traditional remedies of animal, mineral or synthetic origin can be expected.

As in other countries, Germany had already a levelled 3 class system (full MA, WEU, traditional MP) for herbals under medicine law. For historical and market size reasons it may have influenced the European process noticeably (Table 1). But there exist also some specific exemptions such as "Standardzulassungen" (specialities), which are standard market authorisations without need for a single case MA procedure (German peculiarity of common/traditional remedies, §36 AMG). These standard preparations can be e.g. non-industrially produced (licensing for the manufacturer not necessary etc.) and sold outside pharmacies as for instance drug stores or supermarkets. Also homeopathic remedies had already a simplified registration procedure (§38-39 AMG). The new traditional use category might establish another option for homeopathic manufacturers, provided that the product is obviously more than 30 years on the market and health claims may strengthen the market position.

Last but not least exists a large variety of food supplements containing mixtures of vitamins, minerals etc. plus herbal substances, which fall under a less restrictive food law (LMBG). This means that only notification at the Federal Institute for Consumer Protection and Food Safety (Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, BVL) including submission of sample and mock-ups is required but no registration or marketing authorisation (§ 5 of Verordnung über Nahrungsergänzungsmittel = NemV). Often vitamins/minerals get a dummy function in order to avoid the regulatory burden of pharmaceutical law. Food supplements which contain the same ingredients in similar or lower concentrations of HMP reach frequently the market. Consequently, pharmaceutical SMEs -facing competition by cheap uncontrolled products- support the work of authorities to observe the market. Manufacturers and wholesalers of food supplements are often challenged legally and have to justify the priority of food over medicine. Hence, the market control is partly performed by self-regulating forces with considerable impact of regional courts. This competition between highly regulated expensive HMP and low regulated cheap food supplement has been increased, since herbal medicine, apart from very few exemptions, are not any longer reimbursed by health insurances. Furthermore the high price sale of HMP via pharmacies is increasingly challenged by drugstores, supermarkets and the internet market.

Nevertheless it will be likely interesting for manufacturers to access the market with "European traditionals" as an alternative to well-established-use bibliographic procedures. The justification of the traditional use in Europe will be in some cases easier than the reference to consolidated monographs or generation of own data, specifically when deviating from WEU monograph standards. However, it may also happen that a product -listed according to the national §109a- has been sold for more than 30 years, but changes of compounds or increase of concentrations for instance would exclude the automatic transfer to an European THMP. In summary, the new borderline between WEU (German/European) and THMP and the transitional borderline between "German traditional" and "European traditional" product with differing conditions is the prominent concern for the small and medium phytopharmaceutical industry. Product history and existing data, as well as toxicity potential and market strategy including heath claims and distribution paths will determine the regulatory strategy case by case (Roether, 2006; BfArM website).

3 THE PROBLEMATIC DEAL WITH OLD LICENSING CATEGORIES – THE TRANSITION IN SPAIN

Spain represents countries with a complicated situation, although "herbals" are treated formally in two categories: either as "real MP" with all MA requirements but also HP specific bibliographic applications or, the traditional ones, with less quality, safety and efficacy standards. The first mentioned is practically fractional in comparison to the amount of traditional HMP based on several exemption pathways.

Basically, herbal products (defined in Article 42, paragraph 1 of the Spanish Medicines Law 25/1990) with a particular therapeutic/pharmaceutical activity are considered as MP as defined in Article 8.1. of 25/1990. Therefore manufacturing, distribution and sale of these products must follow the same pharmaceutical rules as any other MP. Pharmacological, toxicological and clinical studies may be in principle replaced by bibliographic documentation for non-prescription MP. These so called E.F.P. products (Especialidad Farmacéutica Publicitaria) according to the Ministerial order of 17/09/1982 are extract-based HP which are transferred now into the European WEU category.

Additionally, article 42, paragraph 3 of 25/1990 mention "traditional plants considered as medicinal", but it refers just to the sale (freely but not ambulant) not restricted to pharmacies when no therapeutic claims are made, but without a clear definition or listing. This Law also distinguishes between Herbal Medicinal Products and "Phytotraditional Medicinal Products" in Title X article 117 (fees for MA), again without giving definitions or listings.

Preparations consisting solely of one or more medicinal plants or parts of plants in a cut or powdered state must be included in the Special Register of Medicinal Plants of the AGEMED established in the Ministerial Order of 03/10/1973 and usually referred to as P.M. products (planta medicinal). Similarly to E.F.P. also P.M. products are characterised by quality documentation, bibliographic safety/efficacy data, exclusive sale in pharmacies and possible health claims.

Exempted from this are those preparations that contain just one species and included in the Annex of the this Ministerial Order of 03/10/1973 (without indications): "medicinal plants and their preparations (as single species) without an indication claim that are included in an Annex, do not need to register and no indication claim may be made." In this case, it is sufficient with an administrative notification following the terms of the Royal Decree 3176/1983. The 1973 annex of 110 plants has been officially updated only once in 1976. But it was possible to apply for the inclusion of medicinal plants or its parts. This has been happening without official publication throughout the years containing now around 170 species.

In addition, with the order SCO/190/2004 a negative list amends the Annex with toxic plants whose sale to the public is prohibited or restricted. Acute specific risks associated with some herbs are also addressed by public statements (mensajes publicitarios). A regulation for industrially produced homeopathic compounds exists with the Royal Decree 2208/1994.

Outside medicine law With the Royal Decree of 16/11/1983 (Regulation on manufacturing and trade of 23 vegetal species of use in food) the registration of the most common herbal teas has been located under responsibility of the Ministry of Agriculture, i.e. outside medicine law. Unfortunately the majority of these 23 plants are also included in the described list of herbal species for medicinal use under AGEMED responsibility. There is no clear demarcation between foodstuff and medicine which should be determined in each case by the intention of use. Apart from that, food supplements were traditionally not defined in the Spanish law and could therefore not compete with (traditional) HP of other categories. First regulation started with the EU directives in the 90s. Whereas E.F.P. and P.M. products and all other listed species reap the benefits of graded but relatively low market barriers, other herbal products of non-listed species are per se considered as pharmaceuticals with the elaborative authorisation procedure. Plant extracts containing products , such as guaraná, ginseng, or passiflora, which are legally marketed as food supplements in other MS, could however not be imported into Spain. Already imported supplements are frequently withdrawn from the national market. This has lead to complaints from importing food supplement companies and formal legal action. In March 2007 the European Commission has even decided, to take Spain to the European Court of Justice for its systematic barrier for the import plant based products from other MS as it is infringing the current rules of the free movement of goods in the internal market. The EC states that the Spanish restrictive interpretation of the relevant law goes beyond what is necessary in terms of public health. (European Commission, 2007)

Summarising, it can be stated that the HP legislation in Spain -as historically developed- generated a series of categories in order to reflect the practical use and associated necessary quality/safety standards. However, due to partial overlapping of these categories and lacking modernisation of the law it is somewhat orphaned and will face a radical change by EU legislation. Although 2004/24/EC will offer a new host for Spanish traditional HP, a major issue for re-classification is that HP, which are considered as medicine, can be distributed only via

pharmacies. In 2004 around 15 manufacturers produced around 300 HMP reaching the market via 20.000 pharmacies. In contrast around 200 small manufacturers of around 4000 HP sold via 3800 herbolerias. Clear demarcation avoiding duplication would leave only 250 out of 410 traded species for free sale in 'herboristerias'. Considering the estimated HP annual turnover of 360 million Euro a political hot potato has to be touched by Spanish regulators which is further aggravated by pressure of food supplement manufacturers of other European MS claiming free access to the Spanish market (Casero, 2003; Ricq, 2004; AGEMED, 2007).

4 CONCLUSIONS

The example of UK, Germany and Spain demonstrate the diversity of regulatory situation for herbal medicine at the starting point of the European harmonisation process - in particular the grey area between foodstuffs and medicine and the borderline between well established use and traditional use. The Directive 2004/24/EC, community monograph/listing systems and other European standards force now the national competent authorities to simplify and harmonise the herbal product market. New regulatory hurdles for herbal medicinal products are justified by the safety argument and the political (and commercial) goal of an unrestricted European market. The consumer/patient should benefit in long term from those regulations, even if partially higher prices can be expected for mainly increased standards. Primarily the major burden is put on national regulators when trying to find pragmatic solutions during the adaptation process. But also manufacturers are obliged to react soon and decide already now for the right strategy within the transition period. The introduction of GMP conform production, complicated quality control of combination products and stability tests with determination of quality relevant markers do not allow further delay in order to complete necessary documents before 2011. Ahead of moaning over additional requirements it should not be forgotten, that national HP will have easy market access across Europe, once they comply with European standards set in community list, monographs and guidelines.

The European harmonisation process is historically the first attempt of HMP regulation at multinational scale. Subsequently a trial and error path will unfold issues and solutions on the way to the right balance between support for local industry, freedom of the market and consumer protection. The attentive observation – facilitated by a transparency of web based information of European and national organisations – may help regulators in Latin America and elsewhere taking decisions for their own countries or regions (e.g. Mercosur). Furthermore any grower, manufacturer or importer of herbal starting materials who envisages the European market should be familiar with the currently changing situation.

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Especial Regulación de Fitomedicinas / Special Issue on Regulation of Phytomedicines

Antecedentes y situación reguladora de la medicina herbaria en Cuba

[Antecedents and current situation of the regulation of herbal medicines in Cuba]

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Abstract

Very few plant species have been studied for medical purposes and we have data about their safety and efficacy only for an even smaller number of them. Most countries don't have a legal framework for the control of herbal medicines, and they adopted different focuses in the authorization and commercialization of gerbil medicines. Cuba has a long tradition of use of medicinal plants since the Spanish colonisation and Traditional Medicine is both recognized and integrated in its National System of Health in the 1990. The State Centre for the Quality Control of Drugs (CECMED) as Regulatory Authority of Drugs of Cuba has the task of both and establishing the framework to assure the quality, the security and the efficacy of the herbal medicines by implementing the necessary policies. It also identifies future needs and anticipates solutions to address these regulatory issues.

Keywords: Cuba, herbal medicines, regulatory affairs.

Resumen

Muy pocas especies de plantas se han estudiado con propósitos médicos y un número menor de ellas tienen estudios realizados sobre su seguridad y eficacia. La mayoría de los países no cuentan con un marco legal para el control de los medicamentos herbarios, adoptándose diversos enfoques en la autorización y comercialización de los mismos. Cuba tiene una tradición de uso de las plantas medicinales desde la época de la colonia española y reconoce la Medicina Tradicional en su Sistema Nacional de Salud en el año 1990. El Centro Estatal para el Control de la Calidad de los Medicamentos (CECMED) como Autoridad Reguladora de Medicamentos de Cuba establece nuevas políticas y el marco legal para asegurar la calidad, la seguridad y la eficacia de los medicamentos herbarios e identifica nuevas proyecciones referidas en este trabajo.

Palabras clave: Cuba, medicamentos herbarios, regulación.

INTRODUCCION

Durante las últimas décadas la utilización de las plantas medicinales y productos que se originan de ellas se han extendido en el mundo y han ganado una gran popularidad, sin embargo, muy pocas especies y productos se han estudiado con fines médicos y un número menor cuenta con estudios realizados sobre su seguridad, eficacia y calidad (Cáceres, 1999). Tampoco existe un marco legal sobre las plantas medicinales y los medicamentos herbarios en la mayoría de los países, adoptándose diversos enfoques en la autorización y comercialización de los mismos (OMS, 2002).

Por los problemas anteriores y teniendo en cuenta la tradición histórica y popularidad sobre el uso de las plantas medicinales y medicamentos herbarios, el Centro Estatal para el Control de la Calidad de los Medicamentos (CECMED) como Autoridad Reguladora de Medicamentos de Cuba ha establecido nuevas políticas y el marco legal para asegurar la calidad, la seguridad y la eficacia de los mismos para proteger la salud de los consumidores.

El presente trabajo tiene como objetivo mostrar algunos antecedentes en Cuba sobre el uso de las plantas medicinales y el trabajo realizado en el marco legal para el registro y control de los medicamentos herbarios, así como algunas proyecciones de trabajo.

DESARROLLO

Antecedentes en Cuba.

En Cuba, la introducción de la Medicina Tradicional comienza en el siglo XV, primero por la colonia española y más tarde por africanos, chinos y yucatecas. No es hasta mediados del siglo XX que alcanza su máxima expresión con el Doctor Juan Tomás Roig, quien identifica 595 especies que eran empleadas por la población cubana para diferentes usos curativos (Roig, 1945) y hace un llamado a la comunidad científica nacional para que se estudien dichas plantas con el objetivo de comprobar su seguridad y eficacia, planteando además la necesidad de desarrollar la industria farmacéutica nacional.

En los años 60 la investigación científica sobre las plantas medicinales comienza a desarrollarse en el país de manera ascendente, aunque de forma aislada por distintos investigadores y más bien con fines académicos.

En los años 70 se inaugura la Estación Experimental de Plantas Medicinales "Juan Tomás Roig" con el objetivo de realizar estudios completos con las plantas medicinales de Cuba, pero no fue hasta la década de los 90 que se establece un Programa Nacional para el Desarrollo y la Generalización de la Medicina Tradicional y Natural con participación de todas las unidades e instituciones de Atención Médica del Sistema Nacional de Salud y otras instituciones de investigación y desarrollo. Posteriormente se crea el Centro Nacional de Medicina Tradicional y Natural quien tiene como función establecer las bases metodológicas necesarias para desarrollar, controlar y evaluar la aplicación del Programa.

En el año 1989 se crea oficialmente por el Ministerio de Salud Pública el CECMED como Autoridad Reguladora de Medicamentos de Cuba, encargado de promover y proteger la salud pública a través de un sistema regulador capaz de garantizar el acceso al mercado de los medicamentos con calidad, seguridad, eficacia e información veraz para su uso racional.

En 1996 fue instituido el Buró Regulatorio para la Protección de la Salud Pública como máxima autoridad estatal para actuar en defensa de la salud, al que se subordina el CECMED y otras entidades para conformar el Órgano Regulador Nacional para la Protección de la Salud.

En el año 2002 se crea el acuerdo No. 4282 del Comité Ejecutivo del Consejo de Ministro que establece las disposiciones para la consolidación en el país de las estrategias de la Medicina Tradicional.

Situación reguladora sobre medicamentos herbarios en Cuba.

El Ministerio de Salud Pública ha elaborado una serie de Normas Ramales sobre especificaciones generales de las drogas vegetales y sobre métodos de ensayo y procesos tecnológicos de extractos fluidos y tinturas con el objetivo de guiar y orientar el trabajo de elaboración y estandarización de los medicamentos herbarios. Se publica en el año 1992 una Guía Terapéutica de Fitofármacos y Apifármacos sobre la base de algunas investigaciones realizadas en Cuba con plantas medicinales cubanas y sobre reportes de la literatura científica y monografías farmacopéicas internacionales. En la misma se incluyen un total de 233 formulaciones de fitofármacos para uso en diferentes indicaciones terapéuticas **(Tabla 1)**

En el año 2000, el CECMED identifica la necesidad de incorporar a los productos naturales dentro de la política de medicamentos, en el proceso normal de registro, control, producción y comercialización, y traza estrategias para tratar los temas relacionados con la política, la seguridad, la eficacia, la calidad, el acceso y el uso racional de los medicamentos herbarios, según las recomendaciones de la OMS. En un principio, la implementación de las estrategias se ha basado fundamentalmente en los dos primeros objetivos, a partir de los cuales, se proporcionarán las bases necesarias para conseguir los objetivos de acceso y uso racional.

Uno de los aspectos más importantes para asegurar la calidad, la seguridad y la eficacia de los medicamentos herbarios lo constituye el registro y control de los mismos. En el año 2002 se establecen por el CECMED los Requisitos para el registro de los medicamentos herbarios (CECMED, 2002) y como parte de la regulación 16/2006 "Directrices sobre Buenas Prácticas de Fabricación de Producto Farmacéutico", el anexo No. 3 de Buenas Prácticas de Medicamentos Herbarios.

El Registro de Medicamentos de Origen Natural de uso humano en la República de Cuba, tiene una vigencia de 5 años, al igual que la Renovación que podrá ser solicitada por períodos iguales y sucesivos 90 días antes del vencimiento del Registro. En caso de modificaciones, el Titular del Registro o fabricante del producto tiene la obligación de solicitar la aprobación de las modificaciones dentro del período de vigencia del Registro del medicamento.

La estructura de los requisitos para el registro de los medicamentos herbarios es la siguiente:

a) **Informaciones generales:** Incluye información general sobre las solicitudes de trámites, los productos que serán o no objeto de inscripción y las categorías (A, B y C) establecidas para estos productos.

Cuadro 1: Categorías de los medicamentos de origen natural en la legislación cubana.

A	*Medicamentos Herbarios Nuevos y Medicamentos Herbarios Tradicionales con una nueva vía de administración y/o indicación*, respaldados por estudios farmacológicos, toxicológicos y clínicos controlados.
B	*Medicamentos Herbarios Tradicionales* respaldados por estudios farmacológicos y toxicológicos y por algunos estudios clínicos realizados (estudios de cohorte, estudios de utilización, caso control, series de casos y publicaciones indexadas).
C	*Medicamentos Herbarios Tradicionales* respaldados por información etnomédica y etnoalimentaria del lugar de procedencia del material vegetal, por documentación tecnocientífica y por estudios de toxicidad aguda.

b) **Términos y Definiciones:** Incluye los términos y definiciones adoptados por el CECMED en este campo, que permiten una mejor comprensión del tema.

c) Documentación de solicitudes de trámites: Este capítulo incluye las cuatro partes que forman la documentación del expediente del medicamento, relacionadas a continuación:

- **PARTE 1. Información administrativa.**
  Incluye los datos generales del solicitante y fabricante, una información general del producto terminado, así como las muestras a incluir del producto terminado, sustancias de referencia, material de envase y material informativo del producto que se desee promocionar.
- **PARTE II. Información Químico-Farmacéutica y Biológica.**
  Se presentan todos los aspectos relacionados con la calidad del producto.
- **PARTE III. Información Preclínica.**
  Incluye los aspectos relacionados con la toxicidad del producto y las propiedades farmacológicas comprobadas.
- **PARTE IV. Información Clínica.**
  Incluye los aspectos relacionados con los estudios clínicos, para demostrar la eficacia, incluyendo los datos clínicos y biológicos más significativos para el establecimiento de la seguridad, para la indicación propuesta y si la dosificación prevista es la adecuada**.**

d) **Anexos:** Incluye los modelos e información que se anexa como parte del contenido de la regulación.

e) **Bibliografía:** Se relacionan las referencias bibliográficas consultadas sobre esta materia.

Las fuentes primarias sobre las que se han desarrollado estos requisitos para el registro y control, han sido las directivas de la OMS y las legislaciones de 15 países de Iberoamérica sobre productos naturales (WHO, 1998, 2001, 2004a, 2004b, 2005; OMS, 1993, 2003; García y Cáceres, 2000; Fuentes *et al*, 2000). Las instituciones implicadas con el cumplimiento de la Regulación que estable los requisitos para el registro y control de los medicamentos herbarios, se presentan en la **figura 1.**
El resultado de la implementación y generalización de la Regulación ha tenido un gran impacto para el trabajo de la Autoridad Reguladora en función del control y regulación de los medicamentos que se comercializan en el país, al disponer por primera vez de una regulación nacional donde se establecen los Requisitos para el registro y control de los medicamentos herbarios de uso humano y ha permitido además servir de guía a las instituciones de investigación y desarrollo, la industria, las farmacias y almacenes en el desarrollo, la evaluación y el control de tales productos. En las unidades de Atención Primaria y Secundaria de Salud, también ha jugado un papel importante la implementación de esta regulación, donde cada vez el acceso a estos medicamentos es mayor y la realización de estudios clínicos que corroboren la eficacia de los mismos va permitiendo su uso racional al mismo tiempo.

Tabla 1. Relación de algunos medicamentos herbarios más utilizados, incluidos en la Guía Terapéutica de Fitofármacos y Apifármacos del Ministerio de Salud Pública de la República de Cuba.

Medicamento herbario	**Especie botánica incluida en su composición**	**Indicación Terapéutica/s**
Crema de Cebolla	*Allium cepae L.*	Cicatrizante y queloides
Tintura de Ajo 20 %	*Allium sativum L.*	Antirreumatico, antifungico, hipoglicemiante.
Extracto de Aloe (Jarabe de Aloe 50 %; Crema de Aloe 25 % y 50%; Ungüento de Aloe rectal)	*Aloe vera L.*	Cicatrizante, antiiflamatoria
Extracto Fluído de Bija	*Bixa orellana L.*	Antiseptico, antiiflamatorio
Extracto Fluido de Caléndula	*Caléndula officinalis L.*	Antiseptico, antiinflamatorio
Tintura de Caléndula 10 y 20 %		
Crema de Ají guaguao	*Capsicum annum L.*	Antirreumático
Jarabe de Cañandonga 20 %	*Cassia grandis L.*	Antianémico, antifúngico
Crema de Cañandonga		
Tintura de Limón	*Citrus aurantifolia C.*	Antiespasmódico
Jarabe de Limón		
Tintura de Naranja Agria 20 %	*Citrus aurantium L.*	Flebotónico, diurético
Jarabe de Naranja dulce	*Citrus sinensis L.*	Diurético, flebotónico
Jarabe de Caña santa	*Cymbopogon citratus D.C.*	Diurética, antihipertensivo, antiinflamatorio.
Crema de Caña santa 5 %		
Extracto Fluído de Eucalipto	*Eucalyptus citriodora H.*	Antiséptico, antitusígeno
Tintura de Hinojo 20 %	*Foeniculum vulgare M.*	Antiespasmódica
Extracto Fluído de Tilo	*Justicia pectoralis J.*	Sedante
Jarabe de Tilo 20 %		
Extracto alcohólico de Quitadolor	*Lippia alba M.*	Analgésico
Tintura de Manzanilla 20 %	*Matricaria recutita L.*	Antiiflamatorio, antifúngico, antiespasmódico
Crema de Manzanilla		
Tintura de Cayeput	*Melaleuca leucadendron L.*	Antiséptico, antiinflamatorio
Tintura de Menta japonesa 20 %	*Mentha arvensis L.*	Antiespasmódico, antiiflamtorio de vías respiratorias
Jarabe de Toronjil de menta	*Mentha piperita L.*	Antiespasmódico
Tintura de Hierba Buena 20%	*Mentha spicata L.*	Antiespasmódico
Tintura de Albahaca blanca 20 %	*Ocimum basilicum L.*	Antiespasmódico
Jarabe de Albahaca blanca		
Extracto Fluído de Te de riñón	*Orthosiphon aristatus B.*	Diurético
Jarabe de Te de riñón 20 %		
Extracto Fluído de Pasiflora	*Passiflora incarnata L.*	Sedante
Tintura de Itamo real 20 %	*Pedilanthus tithymaloides L.*	Estomatitis, gingivitis y afta bucal
Crema de Anamú	*Petiveria alliacea L.*	Antiinflamatorio, hipoglicemiante
Extracto Fluído de Pino macho	*Pinus caribaea M.*	Antifúngico
Jarabe de Caisimón de anís	*Piper auritum H.B.K.*	Antiespasmódico, antirreumático
Extracto fluído de Llantén menor	*Plantago lanceolata L.*	Antiinflamatorio, antiséptico
Colutorio de Llantén major	*Plantago major L.*	Aftas bucales, estomatitis, inflamaciones de la encía
Jarabe de Orégano francés	*Plecthranthus amboinicus L.*	Expectorante, antitusivo
Tintura de guayaba 20 %	*Psidium guajaba L.*	Antifúngico, antidiarréico
Elixir de Guayaba		
Talco de Guayaba		
Melito de Mangle rojo	*Rhizophora mangle L.*	Cicatrizante, antiulcerosa, antiséptico
Jarabe de Romero	*Rosmarinus officinalis L.*	Antiséptico
Jarabe de Salvia de castilla	*Salvia officinalis L.*	Broncodilatador, expectorante
Tintura de Guacamaya francesa 20 %	*Senna alata R.*	Antifúngica
Jarabe de Maíz	*Zea mays L.*	Diurético
Extracto de Jengibre	*Zingiber officinale R.*	Tratamiento de flatulencia, dispepsias, cólicos gastrointestinales vómitos , diarreas.
Tintura de Jengibre		

Tabla 2. Tiempos (en días naturales) establecidos para cada tipo de solicitudes de trámites de registro.

Solicitud Tipo	Inicial	Completamiento de la Documentación		Total
	CECMED	Solicitante	CECMED	
Inscripción A	180	90	105	375
Inscripción B y C	150	90	105	345
Renovación	120	90	105	315
Modificación	120	90	105	315

Tabla 3. Plantas Medicinales que serán incluidas en futuras ediciones de la Farmacopea Cubana de Plantas Medicinales del Ministerio de Salud Pública de la Republica de Cuba.

Especie/s botánica/s	Nombre común	Categoría(s) Terapéutica/s o Indicaciones
Allium cepae L.	Cebolla	Cicatrizante y queloide
Allium sativum L.	Ajo	Antirreumático, antifúngico, hipoglicemiante
Aloe vera L.	Sábila	Cicatrizante, antiiflamatorio, inmunomodulador
Anacardium occidentale L.	Marañón	Antidiarreico, antibacteriano
Anethum graveolens B.	Eneldo	Antiespasmódico
Artemisia absinthium L.	Artemisa	Carminativo, antiespasmódico
Bidens piloso L.	Romerillo	Antiulceroso
Bixa orellana L.	Bija	Antiséptico, antiinflamatorio
Brassica juncea L.	Mostaza de la tierra	Antiinflamatorio
Caléndula officinalis L.	Caléndula	Antiseptico, antiinflamatorio
Capsicum annum L.	Ají picante	antirreumático
Cassia grandis L.	Cañandonga	Antianémico
Citrus aurantifolia C.	Limón	Diurético, flebotónico
Citrus aurantium L.	Naranja agria	Flebotónico, diurético
Citrus nobilis L.	Mandarina	Antigripal
Citrus sinensis L.	Naranja dulce	Diurético, flebotónico
Coriandrum sativum	Cilantro	Cefaleas, úlcera, reumatismo, estomático, carminativo, antiespasmódico, estimulante de secreciones de jugos gástricos, antimicrobiano
Curcubita moschata D.	Calabaza	Antihelmítico
Cúrcuma longa	Yuquilla	Trastornos hepáticos, ictericia, afecciones gastrointestinales y respiratorias, dismenorrea, diabetes
Cymbopogon citratus D.C.	Caña santa	Diurética, antihipertensivo, antiinflamatorio
Erigium foetidum L.	Culantro	Antiespasmódico, tos, antitusivo, emenagogo y febrífuga.
Eucalyptus citriodora H.	Eucalipto de limón	Antiséptico, antitusígeno
Foeniculum vulgare M.	Hinojo	Antiespasmódica
Hibiscus elatus Sw.	Majagua	Antihistamínico
Indigofera suffructicosa M.	Añil cimarrón	Anticonvulsivante, pediculicida
Jasminum officinale L.	Jazmin de 5 hojas	Antihistamínico
Justicia pectoralis J.	Tilo	Sedante
Lepidium virginicum L.	Mastuerzo	Diurético, antirreumático
Lippia alba M.	Quitadolor	Analgésico
Mangífera índica L.	Mango	Antiinflamatorio y antioxidante
Maranta arundinacea L.	Sagú	Diarréico, emoliente, enfermedades de la uretras y la vejiga.
Matricaria recutita L.	Manzanilla	Antiiflamatorio, antifúngico, antiespasmódico
Melaleuca leucadendron L.	Cayeput	Antiséptico, antiiflamatorio
Melissa officinalis L.	Toronjil	Sedante
Mentha arvensis L.	Menta japonesa	Antiespasmódico, antiiflamatorio de vías respiratorias
Mentha piperita L.	Toronjil de menta	Antiespasmódico
Mentha spicata L.	Hierba buena	Antiespasmódico
Morinda citrifolia	Noni	Antiinflamatorio, antihistamínico, antibacteriano
Morinda royoc	Garañón	Antioxidante

Tabla 3 (Continuación). Plantas Medicinales que serán incluidas en futuras ediciones de la Farmacopea Cubana de Plantas Medicinales del Ministerio de Salud Pública de la Republica de Cuba.

Especie/s botánica/s	Nombre común	Categoría(s) Terapéutica/s o Indicaciones
Murraea exotica L.	Muraya	Pediculicida
Mussa paradisiaca L.	Plátano	Pediculicida
Ocimum basilicum L.	Albahaca blanca	Antiespasmódico
Ocimum gratissimum L.	Orégano cimarrón	Antiespasmódica, antimicrobiano, antigripal y febrífuga.
Ocimum tenuiflorum L.	Albahaca morada	Hipoglicemiante
Origanum majorana L.	Mejorana	Flatulencia, diarrea, tónico y sedante del SNC, digestiones lentas.
Orthosiphon aristatus B.	Té de riñón	Diurético
Parthenium hysterophorus L.	Escoba amarga	Champú anticaspa
Passiflora incarnata L.	Pasiflora	Sedante
Pedilanthus tithymaloides L.	Itamo real	Estomatitis, gingivitis y afta bucal
Petiveria alliacea L.	Anamú	Hipoglicemiante, antiinflamatorio
Piper auritum H.B.K.	Caisimón de anís	Antiespasmódico, antirreumático
Piper ossanum C.	Platanillo de Cuba	Antiinflamatorio
Plantago lanceolata L.	Llantén menor	Antiinflamatorio, antiséptico
Plantago major L.	Llantén major	Aftas bucales, estomatitis, inflamaciones de la encía
Plecthranthus amboinicus L.	Orégano francés	Expectorante, antitusivo
Protium cubense R.	Copal	Antiinflamatorio antiséptico
Psidium guajaba L.	Guayaba	Antifungico, antidiarréico
Rhizophora mangle L.	Mangle rojo	Cicatrizante, antiulcerosa, antiséptico
Rosmarinus officinalis L.	Romero	Antiséptico
Ruta graveolens L.	Ruda	Sedante
Salvia officinalis L.	Salvia de castilla	Broncodilatador, expectorante
Senna alata R.	Guacamaya francesa	Antifúngica
Stachytharpheta jamaicensis (L) Vahl	Verbena cimarrona	Antiparasitario, afecciones renales y de la piel, antimicrobiano.
Tamarindus indica L.	Tamarindo	Antiinflamatorio
Thymus vulgaris L.	Tomillo	Afecciones respiratorias agudas y crónicas
Xanthium occidentalis	Guisazo de caballo	Diurético
Zea mays L.	Maíz	Diurético
Zingiber officinale R.	Jengibre	Problemas digestivos, tonificante

Hasta la fecha el CECMED ha registrado un total de 60 medicamentos herbarios nacionales y de importación que se producen en la industria. Los medicamentos que se elaboran de manera semi-industrial, que son la mayoría de los que se producen en el país en los centros de producción local y dispensarios farmacéuticos, con condiciones tecnológicas y recursos materiales mínimos, relacionados en la **tabla 1**, siguen otros requisitos establecidos en la Regulación 29/2000 "Requisitos para las solicitudes de autorización de uso de medicamentos de origen natural de uso humano, de producciones locales y dispensariales", para su autorización que están específicamente relacionados con la calidad del producto y que responden a productos que se elaboran a partir de un listado de plantas autorizadas para el cual se tuvo en cuenta la tradición de uso en Cuba con fines medicinales y las investigaciones realizadas en el país y otros reportes de la literatura científica sobre seguridad y eficacia.

Los tiempos establecidos en el reglamento de registro para las solicitudes de trámites de inscripción, renovación y modificación en el registro, se presentan en la **tabla 2**.

Proyecciones de trabajo

El CECMED ha establecido proyecciones de trabajo con el objetivo de perfeccionar la base legal para la regulación de medicamentos herbarios con la elaboración y actualización de pautas, directrices técnicas y metodologías nacionales para evaluar la seguridad, la eficacia y la calidad de las plantas medicinales y medicamentos herbarios, entre las que se pueden mencionar, guías sobre métodos de ensayos para el control de la calidad, guía sobre especificaciones de calidad y criterios de aceptación

de las drogas vegetales y productos terminados y metodologías para la investigación de las plantas medicinales. Estos documentos serán elaborados teniendo en cuenta las directrices de la OMS y nuestras condiciones de trabajo. También está en ejecución el proyecto de elaboración de las monografías de las plantas cubanas que formarán parte de la primera edición de la Farmacopea Cubana de Plantas Medicinales con las especies relacionadas en la **tabla 3**, así como la elaboración de las buenas prácticas agrícolas, de recolección y de conservación de las plantas medicinales. Otra de las proyecciones está relacionada con el desarrollo de las pautas para el consumidor sobre la información necesaria para el uso correcto de las plantas medicinales.

CONCLUSIONES

- Cuba integra la Medicina Tradicional en el Sistema Nacional de Salud y crea en el año 1995 un Programa Nacional para el Desarrollo y Generalización de la Medicina Tradicional.
- El CECMED como Autoridad Nacional Reguladora de Medicamentos, en el año 2000, traza algunas estrategias de trabajo para asegurar la calidad, la seguridad y la eficacia de las plantas medicinales y medicamentos herbarios.
- Se implementa y perfecciona el marco legal para el registro y control de los medicamentos herbarios a partir del año 2002.
- Se trazan proyectos de elaboración de documentos regulatorios relacionados con las buenas prácticas agrícolas, de recolección y conservación de las plantas medicinales, sobre la calidad, la seguridad y la eficacia de los medicamentos herbarios y sobre las pautas para el consumidor sobre la información necesaria para el uso correcto de las plantas medicinales.

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Especial Regulación de Fitomedicinas / Special Issue on Regulation of Phytomedicines

Phytomedicines in Jamaica: regulatory issues

[Fitomedicinas en Jamaica: regulación]

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Abstract

Jamaica is making its way towards a full regulation of herbal medicines and related products, namely food supplements. This has been pushed by the increasing imports of unregulated herbal products into the Island creating a need for protecting both our citizens and local producers alike. From a practical legal point of view the current legal framework was based mainly in the Food and Drug Act 1964, and the Food and Drug Regulations 1975, established by the Ministry of Health, but they did not refer to herbals and herbal medicines in its contents. From 1999, Jamaican governmental and private institutions are working on the amendment of these acts and participating actively in international workshops to regulate phytomedicines both within the country and the Caribbean/Centro American region. However the law will force growers to perform adequate laboratory tests that are often out of their economical reach, and the help of the administration has been proposed to solve this problem. Despite theses developments the answer to "what is the status on the Amendment?" is still in limbo.

Keywords: Jamaica, herbal medicines, regulatory affairs.

Resumen

Jamaica esta haciendo progresos hacia la regulación completa de los medicamentos herbarios y productos relacionados como los suplementos alimentarios. Esto ha sido impulsado por el aumento de importaciones de productos herbarios no regulados en la isla, lo que creo una necesidad de proteger tanto al consumidor como al productor local. Desde un punto de vista practico el marco legal basado en la Ley de Alimentos y Medicamentos de 1964 y las Regulaciones de Alimentos y Medicamentos de 1975, establecidas por el Ministerio de Salud, pero estas no hacían mención de los productos herbarios. Desde 1999, el gobierno jamaicano e instituciones privadas trabajan en la actualización de estas leyes por enmienda, además de participar activamente en grupos de trabajos internacionales para regular tanto la situación interna como la regional (Caribe/Centroamérica). Sin embargo la regulación del mercado herbario forzara a los productores locales a realizar análisis que están fuera de su capacidad económica, y la ayuda estatal ha sido propuesta como solución. A pesar de todos estos avances la respuesta a la situación de la enmienda se encuentra aun en el limbo.

Palabras clave: Jamaica, medicamentos herbarios, regulación.

INTRODUCTION

Herbs are always difficult to characterise because of their complexity of active ingredients or compounds that are usually not known. History has shown that multiple choices exist for protecting human health. Since 1994 the revived interest of natural products as preventative and therapeutic agents accompanied by the high demand for natural remedies and herbals have drawn the attention of the Ministry of Health in Jamaica.

The Ministry has a responsibility to protect the health of citizens, and therefore has to set laws to govern the registration, importation, manufacture, storage, distribution, sale and use of herbal medicinal products. The Food and Drug Act 1964, and the Food and Drug Regulations 1975, established by the Ministry of Health did not refer to herbals and herbal medicines in its contents.

DEFINITIONS BY LEGISLATION SECTION 2- JAMAICA FDA

Food- "any article used for food or drink by man, including chewing gum and any ingredient that may be mixed with food or drink for any purpose."

Drug- "any substance or mixture of substance manufactured, sold or represented for use in the diagnosis, treatment, mitigation or prevention of disease, disorder, abnormal physical state or symptoms thereof in man or animal; restoring, correcting or modifying organic functions in man or animal; dis-infection in premises in which food is manufactured, prepared, preserved, packaged or stored for sale or sold for control of vermin or insects in such premises."

The regulations pursue to address two important issues related with herbal medicines: Quality and Efficacy. Q*uality* is an asset. The primary reason why standardization exists for herbal extracts is to achieve as much control in clinical double blind studies as possible. It is also to protect consumer interests specially relating to product claims and maintain requisite standards-batch to batch consistency. *Efficacy* is the ability to effect label claim-indication/action, identifying the pharmacological activity, the potency for effective doses and to justify the claims on the labels.*Safety* contributes to improve the quality of life. Safety is the fundamental principle and the critical component of quality management. There is the common misconception that all natural products or plants are safe! Safety eliminates/ control toxicity and drug interactions. Today good agricultural practices (GAP) are now in place so as to avoid growing where the soil is contaminated with heavy metals, as well as collection of the wrong species and adulteration with other herbs.

THE CURRENT STATE OF THE INDUSTRY

In 1994, the Ministry of Health (MOH) saw the necessity to intervene in the escalating importation of herbal materials and dietary supplements by treating these as "drugs". The Wholistic Herbal Association (WHA), which was founded by this author among other stakeholders and consumers in the industry, took the M.O.H to task to prove if an "herb" is a drug or a "food". The Association engaged the Ministry into a legal tangle along with media "war" with the medical practitioners during 1995-1999. The former Chairman Dr. Robertson and the former President Dr. Vance Lannaman NMD, along with the stakeholders in the industry lobbied with the M.O.H before the Houses of Parliament.

On March 22nd 1999, the Honourable Houses of Parliament took a decision that a special committee of members of the Association and "The Joint Select Committee on Human Resources and Social Development" (appointed by the Houses of Parliament and the Ministry of Health) met for one year preparing documentation to be submitted to Parliament to amend the FDA 1974 to include the following:

1. Herbal Remedies
2. Health Foods
3. Herbs
4. Finished Herbal Products
5. Herbal Materials
6. Dietary Supplements
7. "Over-The-Counter" OTC herbal products.

The document was prepared and submitted to the Permanent Secretary in the M.O.H for perusal and submission to the Chief Parliamentary Council. In 2000 the Ministry of Health appointing a representative of each complementary medicinal therapy, formed an Advisory Panel for Complementary Medicine. Dr. Sonia Davidson MD. was appointed by the M.O.H as the Chairman.

On November 13-16 2000 the Ministry of health hosted a Regional Meeting on Herbal Medicine, which was held in Jamaica. Participants from Barbados, Brazil, Canada, Chile, Guatemala, Jamaica, Mexico, Panama, USA and representatives from PAHO /and World Health Organisation all attended. This meeting was an opportunity for drug regulators of various countries to come together to discuss the different issues surrounding the production, registration and use of herbal products and to develop a proposal on harmonized standards and regulations to assure safe safety and quality of products in share markets. It was also hoped that experiences of countries from other regions would serve as reference and guide for the discussion (Pan American Health Organization, 2002.).

The Advisory Panel completed a document on procedures to harmonise with Complementary Alternative Medicine, which included the operations of herbal practitioners and therapists to be regulated. To date the amendments for Phytomedicines and the Practitioners of Complementary Medicine have not been included in the FDA amendments, or submitted for approval by the Honourable Houses of Parliament.

PRESENT REGULATORY FRAMEWORK

After a period of four years the changes of the Regulatory framework have been completed, and submitted to the Chief Parliamentary Council for adjustments since late 2006, but still no amendments are in place. The Ministry of Health has made reference taken by competent authorities in Australia, Canada, Germany, England and the United States, references to WHO guidelines on the assessment of herbal products and definitions were also adapted for use (WHO. 1998, 2001, 2004a., 2004b).

There is not a Jamaican Pharmacopoeia in place. *The British Pharmacopoeia* (British Pharmacopoeial Commission, 2008) is instead required to be in all Pharmacies in the island. *In addition,* References can be made from *"The Complete German Commission E Monographs"* (Blumenthal et al., 1999) published by the American Botanical Council which also includes some Canadian herbal references.

The Pharmacy Council in Jamaica has also made requests for their Laws to be amended to make it possible for herbals to be sold in "special shops" which would be regulated by the Pharmacy Council. This too has not yet been amended.

Since 2005 the Director of Standards and Regulation MOH and their officials along with representatives of Complementary Medicinal Practitioners met formerly on a monthly basis, but this has fell down tremendously.

Documentation Requirements for Registration of Herbal Remedies

It is interesting that the application form from the Pharmaceutical and Regulatory Affairs unit is still under the *Registration of Herbal products, food and drugs* Act of 1964.

This form has to answer pertinent questions such as a statement of content of the product, the posology, rationale for combinations, toxic/side effects, tests to conform quality and potency.

Attached to the form must be:

- A"*Certificate of Free Sale*" that must be endorsed by the Jamaican Consulate in the country of origin.
- *A "Certificate of Analysis*" indicating tests for quality and potency.
- Five samples of the product with the labels indicating manufacturer, expiry dates, and batch numbers.

A fee of J$5000.00 (approx. U$71.00) applies.

Table 1. Herbs and by- products restricted by the M.O.H. for importation.

Common name	Latin name
Chaparral	*Ceanothus* spp.
Comfrey herb	*Symphytum officinale*
Germander	*Teucrium chamaedrys*
Willow Bark	*Salix alba*
Yohimbe	*Corymanthe yohimbi*
	Pausinystalia johimbe
Lobelia	*Lobelia inflata*
Magnolia	*Magnolia glauca*
Ephedra, Ma Huang	*Ephedra sinica*
Kava Kava	*Piper methysticus*

The Requirements for Health Foods

Health food must comply with a simplified procedure to be registered in Jamaica:

- Evaluation and review of active ingredients and concentration.
- Verification of label claims, purity –certificate of Analysis.
- Five samples of products
- Proof of approval in country of origin.
- Scientific support claims may be requested.

All products are regulated except:

- Homeopathic preparations more dilute than 1-1000 fold dilution of a mother tincture.
- Herbal Teas except where there are claims.
- Products, which exist and function principally as food if they make no therapeutic claims e.g. garlic. (*Allium sativa*). Fees are required for passive assessment.

Several restrictions apply to this category. First of all injectable presentations are not allowed and they can only be registered as prescription drugs. Secondly, there is a list of herbs and by- products are restricted by the M.O.H. for importation. Restriction is based on "advisory reports "received from other international regulatory bodies (see Table1 for a list of restricted plant species).

OUR CHALLENGES

The need for an adequate laboratory support for testing our raw materials to acquire a Certificate of Analysis is most challenging for growers of raw materials. At present our Scientific Research Council is planning assistance in this area. This would assist the many applicants to provide requisite documentation for product approval.

The questions asked daily by stakeholders is "what is the status on the Amendment?" Its answer is still in limbo.

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An Overview on the Development in Regulation and Control of Medicinal and Aromatic Plants in the Indian System of Medicine

[Una panorámica del desarrollo de la regulación y control de plantas medicinales y aromáticas en el sistema indio de medicina]

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Abstract

India have well-recorded and well practiced knowledge of traditional herbal medicines under indigenous systems of medicine like Ayurveda, Siddha and Unani. On the other hand, with about 6000 plants representing about 75% of the medicinal needs of the third world countries India is a major worldwide exporter of raw medicinal and aromatic plants and processed plant-based drugs. Government of India has taken various initiatives to improve the herbal drug standards and promote Indian system of medicine. Government of India has been stiffening the herbal drug regulations from time to time by establishing various bodies to control the manufacture and sales of herbal drug. It is continuously taking various corrective measures by implementing certain acts and rules coping with the developing global standards for natural products. A recent major move has been the convertion of The Department of Indian Systems of Medicines and Homoeopathy (ISM & H) established in 1995 into the Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH) in 2003. The Department made steady progress since them and emphasis was laid on implementing the schemes which address the thrust areas identified by the Department like up gradation of educational standards, quality control and standardization of drugs, improving the availability of raw material, research and development and awareness generation about the efficacy of the systems domestically and internationally.

Keywords: India, herbal medicines, regulatory affairs, Ayurveda, Yoga, Naturopathy, Unani, Siddha.

Resumen

India tiene un uso de medicinas herbarias tradicionales bien documentado y bien establecido bajo diversos sistemas indígenas como el Ayurveda, Siddha y Unani. Por otro lado, con mas de 6000 especies de plantas representado el 75% de las necesidades medicinales de países del tercer mundo, India es un exportador mundial de drogas vegetales y especias. El gobierno hindú ha tomado varias iniciativas para mejorar y endurecer las normas de calidad en el sector y establecer varios organismos de control de su producción y venta. También esta continuamente tomando medidas correctivas mediante la implementación de leyes y regulaciones tomadas de organismos reguladores internacionales. La mas reciente e importante accion ha sido la reconversión del Departamento de sistemas Indios de medicina y homeopatia, establecido en 1995, en el Departamento de Ayurveda, Yoga y Naturopatia, Unani, Siddha y Homeopatía (AYUSH) en 2003. Este departamento a hecho progresos continuos en la regulación de sistemas tradicionales con énfasis en aumentar los niveles de educación, control de calidad y estandarización de drogas, aumentando la disponibilidad de materiales crudos, investigando y desarrollando así como concienciando de la eficacia de los sistemas tradicionales tanto a nivel domestico como internacional.

Palabras clave: India, medicamentos herbarios, regulación, Ayurveda, Yoga, Naturopatia, Unani, Siddha.

INTRODUCTION

Despite the achievements of synthetic chemistry and the advances towards rational drug design, natural products continue to be essential in providing medicinal compounds and as starting points for the development of synthetic analogues. In some particular cases, such as antitumor and antimicrobial drugs, about 60% of the medicines currently available on the market and most of those in the late stages of clinical trials are derived from natural products, mainly from higher plants (Calixto, 2000). With the increasing power of screening programs and

the increasing interest in the reservoir of untested natural products, many future drug developments will be based, at least in part, on natural products.

India is having a well-recorded and well practiced knowledge of traditional herbal medicine (Kamboj, 2000). Medicinal herbs have been in use in one form or another, under indigenous systems of medicine like Ayurveda, Siddha and Unani. India is a major exporter of raw medicinal and aromatic plants and processed plant-based drugs. It is generally estimated that over 6000 plants in India are in use in traditional, folk and herbal medicine, representing about 75% of the medicinal needs of the third world countries (Dubey et al., 2004; Mukherjee, 2002a). India, with this traditional background, needs to increase its share in the world market. The US market is expected to grow to 5 trillion US dollars in 2050 (Joshi et al., 2004; Rai et al., 2006). This can be achieved by judicious product identification based on diseases found in the developed world for which no medicine or only palliative therapy is available; such herbal medicines will find speedy access into those countries. Also, harmonization and improvement in the processes of regulation is the need of the day, since it will be possible for the people to obtain high quality herbal medicines (Calixto, 2000; Verproote, 2005). In this context, India has acknowledged the need for addressing the issue of the use of herbal medicines along with other regulatory measures.

Not many nations have launched initiatives to inculcate traditional herbal regulatory measures into their drug regulatory system. In the herbal boom world wide it is estimated that high quality phyto-medicinals will provide safe and effective medication and people engaged therein should have wide knowledge in every respects of the production and utilization of herbals. In this context quality control of botanicals has been given priority on which several guidelines have been reported. (Mukherjee, 2002b). In India, separate Department or the Indian System of Medicine and Homeopathy (ISM & H) has been made who are specially dealing with the rules and regulations for the herbals along with the Drugs and Cosmetic act and rules which has come up with the rules for the implementation of GMP in herbals, which will not only help to make the quality herbal products but also to safeguard the adverse effects of the herbals too. An attempt has been made to make a complete review on every aspect of the development in the regulations of Indian System of Medicine.

THE ANCIENT INDIAN TRADITIONAL MEDICINE

The World Health Organization (WHO) estimates that about 80% of the populations living in the developing countries rely almost exclusively on traditional medicine for their primary health care needs. India has an ancient heritage of traditional medicine. India possesses a well-recorded and traditionally well-practiced knowledge of herbal medicine. It is generally estimated that over 6000 plants in India are in use in traditional, folk and herbal medicine, representing about 75% of the medicinal needs of the world countries. *Materia medica* of India provides lots of information on the folklore practices and traditional aspects of therapeutically important natural products. Indian *Materia medica* includes about 2000 drugs of natural origin almost all of which are derived from different traditional system and folklore practices. Out of these drugs derived from traditional system, 400 are of mineral and animal origin while the rest are of vegetable origin. Three of the ten most widely selling herbal medicines in the developed countries, namely preparations of *Allium sativum, Aloe barbedensis* and *Panax* sp. are available in India. It mainly consists of three major systems namely Ayurveda, Siddha and Unani (ASU). With the emerging interest in the world to follow Indian system of Medicine, the government of India is trying their best to bring out therapeutic approaches available in original system of medicine as well as help in generating data to put these products on national health care program (Mukherjee, 2002b, 2003a,2006).

Ayurveda

Ayurveda is a system of healing from India. The origin of Ayurveda has been lost in prehistoric antiquity, but their characteristic concepts appeared to have been nurtured between 2500 and 500BC in India (Mukherjee, 2001). Ayurveda is usually translated as “the science of life” (Anonymous, 2006a). In Indian system of traditional medicine, it is accepted as the oldest written medical system that is also supposed to be more effective in certain cases than modern therapies. Formulations and dosage forms have great importance in Ayurveda. Generally Ayurvedic formulations are multi-component mixtures containing plant and animal derived products, minerals and metals. During the Samhita period (1000 BC), Ayurveda developed into eight branches of specialties. Whereas, during the last 50

years it has developed into twenty-two specialties. Despite the increasing popularity of herbal medicines and herbal cosmetics abroad, it would seem that Ayurveda is yet to gain wider acceptance among medical scientists internationally (Mukherjee et al., 2005a; Mukherjee, 2003b). Ayurveda is effective in the hands of an experienced practitioner, and most of the herbs used are fairly safe. Unfortunately, lack of regulation, quality issues in some products has led to serious concerns about the safety of ayurvedic medicines.

Siddha System of Medicine

Siddha system is one of the oldest systems of medicine in India, which blends medicine and mysticism. The word Siddha was coined from word 'Siddhi', which means attainment of perfection and the art was mastered, practiced and teached by wise men known as 'siddhars'. Although Siddha medicine resembles the aspects of Ayurveda, they possess different origin. Siddha medicine originated from the south of Indian subcontinent rather than the north. The diagnosis of diseases involved identifying its causes. Identification of causative factors is through the examination of pulse, urine, eyes, study of voice, color of body, tongue and the status of the digestive system. The Siddha system of medicine emphasizes that medical treatment is oriented not merely to disease but has to take into account the patient, environment, the meteorological consideration, age, sex, race, habits, mental frame, habitat, diet, appetite, physical condition, physiological constitution etc. This means the treatment has to be individualistic which ensures lesser chance of committing mistakes in diagnosis or treatment.

Unani System of Medicine

Unani Tibb (*Unani* means Greek [Ionnian] and *Tibb*, from the Arabic, means medicine) is a system of medicine practiced today in the South Asian countries of India, Pakistan, and Bangladesh. Its origins lie in ancient Greek, Arabic, and Persian medicine. In India, Arabs introduced the Unani system of medicine, which was developed by the Mughal emperors who invaded India. (Williamson, 2006; Mukherjee and Wahile, 2006). Here diseases are considered as a natural process and its symptoms are the reaction of the body to the diseases. Unani, with its humoral philosophy, views nature and mankind as ideally coexisting in a balanced manner. Specifications for a range of behaviors and events that could lead to sickness and disease are outlined in the Unani texts. In common with many traditional sources of medicine, Unani-Tibb emphasizes the use of flavors and tastes to adjust the imbalances which contribute to disease. The choices of foods and the manner in which they are prepared are considered to be among the most important issues to consider when choosing a diet to improve or maintain health (Grotte, 2004; Mukherjee, 2005b). Skillful use of warming and cooling spices and herbs contribute heavily to the appropriateness of the meal to correct the root causes of imbalances.

With the emerging interest in the world to adopt and study the traditional system and to exploit their potentials based on different healthcare systems, Government of India is exploring several possibilities for the evaluation of these systems to bring out therapeutic approaches available in original system of medicine as well as to help in generating data to put these products on national health care program. The Indian herbal products including Ayurveda, Unani, Siddha and Homeopathy are regulated under the Drugs & Cosmetics Act and licensing of such products remains a state subject. Provision relating to the regulatory aspects of natural products manufacture and control has been prescribed in Drugs and Cosmetics Act 1940, Govt. of India; various aspects of the regulation on control of herbal medicinal products has been described in Table 1.

DEPARTMENT OF AYURVEDA, YOGA & NATUROPATHY, UNANI, SIDDHA AND HOMOEOPATHY (AYUSH)

The Department of Indian Systems of Medicines and Homoeopathy (ISM & H) established in Ministry of Health & Family Welfare in March, 1995 was renamed as the Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH) in November, 2003. The Department made steady progress during the year 2005-2006. Emphasis was laid on implementing the schemes which address the thrust areas identified by the Department like up gradation of educational standards, quality control and standardization of drugs, improving the availability of raw material, research and development and awareness generation about the efficacy of the systems domestically and internationally (Anonymous, 2006b; Anonymous. 2003a).

Table 1: Regulatory aspects of natural products based on Drugs and Cosmetics Act of India

Item	Section	Criteria
Misbranderd drugs	33 E	ASU drugs are deemed to be misbranded: ✓ If colored or coated to conceal the damage or made appear better than therapeutic value ✓ If it is not labeled in prescribed manner ✓ If label or container accompanying drug bears any false claim or misleading.
Adulterated drugs	33EE	ASU drugs are deemed to bne adulterated ✓ If it consists filthy, or decomposed material ✓ If prepared, packed or stored under insanitary conditions ✓ If its container contains any poisonous or deleterious substance ✓ colour other than one which is prescribed ✓ harmful or toxic substance ✓ If any substance mixed to reduce its quality or strength.
Spurious drugs	33EEA	ASU drugs are deemed to be spurious ✓ If it is sold or offered under another name. ✓ If it is an imitation or substitute for another drug ✓ If the label or container bears the name of an individual or company which is fictious. ✓ If it has been substituted by other drug
Regulation of manufacture for sale of ASU drugs.	33EEB.	No person shall manufacture for sale or distribution, any ASU drug except in accordance with prescribed standards.
Prohibition of manufacture and sale of certain ASU drug.	33EEC.	No person shall manufacture ASU drugs which are: ✓ misbranded, adulterated or spurious ✓ patent or proprietary medicine, ✓ contravention to any of the provisions of the act
Power of Central Government to prohibit manufacture of ASU drugs in public interest.	33EED.	Central govt. can prohibit manufacture of ASU if: ✓ Drug involve any risk to human beings or animals ✓ Drug does not have the therapeutic value claimed
Government Analysts.	33F.	Central or State govt. can appoint any person with the prescribed qualification and do not have any financial interest in ASU drug.
Inspectors.	33G.	Central or State govt. can appoint any person with the prescribed qualification and do not have any financial interest in ASU drug.
Penalty for manufacture, sale, etc., of Ayurvedic, Siddha or Unani drug in contravention of this Chapter.	33I	manufactures for sale or for distribution of any ASU drugs deemed to be adulterated or without a valid licence as required.
Penalty for subsequent offences.	33J.	Shall be punishable with imprisonment for a term not less than two years but which may extend to six years and with fine not less than 5000 INR.
Confiscation.	33K.	Any person convicted under the act, the respective stock of ASU drug can be confiscated.
Cognizance of offences.	33M.	▪ No prosecution under this Chapter shall be instituted except by an Inspector. ▪ No Court inferior to that of a [Metropolitan Magistrate] or of a [Judicial Magistrate] of the first class shall try an offence punishable under this Chapter.
Power of Central Government to make rules.	33N	The Central Government may -after consultation with, or on the recommendation of, the Board- and after previous publication by notification in the Official Gazette, make rules for the purpose of giving effect to the provisions of this Chapter:
Application for licence to manufacture Ayurvedic (including Siddha) or Unani drugs.	153	An application for the grant or renewal of a licence to manufacture for sale any ASU drugs shall be made in Form 24-D to the Licensing Authority along with a fee of rupees sixty.
Form of licence to manufacture Ayurvedic (including Siddha) or Unani drugs:	154.	Subject to the conditions of rule 157 being fulfilled, a licence to manufacture for sale any ASU drugs shall be issued in Form 25-D.
Loan Licence.	153-A.	An application for the grant of renewal of a loan licence to manufacture for sale of any ASU drugs shall be made in Form 25-E to the Licensing Authority along with a fee of rupees thirty.
Certificate of award of G.M.P. of Ayurveda, Siddha and Unani Drugs.	155 B	shall be issued to licensees who comply with the requirements of GMP of ASU drugs as laid down in Schedule T.
Standards to be complied with in manufacture for sale or for distribution of Ayurvedic, Siddha and Unani Drugs.	168.	***Single drugs***: The standards for identity, purity and strength as given in editions of Ayurvedic Pharmacopoeia of India. ***Asavas and Arishtas :*** The upper limit of alcohol as self generated alcohol should not exceed 12% v/v.

Department of AYUSH drafted certain rules further to amend the Drugs and Cosmetics Rules, 1945 in the Gazette of India. The draft claims that the certificate of Good Manufacturing Practices (GMP) to manufacturers of Ayurveda, Siddha or Unani drugs shall be issued to licensee who comply with the requirements of Good Manufacturing Practices (GMP) of Ayurveda, Siddha and Unani drug as laid down in Schedule T (Mukherjee et al., 2003c).

The Good Manufacturing Practices (GMP) is prescribed to ensure:

i. Raw materials used in the manufacture of drugs are authentic, of prescribed quality and are free from contamination.
ii. The manufacturing process is as has been prescribed to maintain the standards.
iii. Adequate quality control measures are adopted.
iv. The manufactured drug which is released for sale is acceptable quality.

To achieve the objectives listed above, each licensee should follow the prescribed process of manufacture of drugs which should be documented as a manual and kept for reference and inspection.

FACTORY PREMISES

The manufacturing plant should have adequate space for receiving and storing raw material, manufacturing process areas, Quality Control section, finished goods store, office, rejected goods/drugs store. It also gives directives for herbal industries regarding the Location and surroundings, buildings, water Supply, disposal of waste, container's cleaning, stores, raw materials, packaging materials, finished goods stores, working space, health clothing, sanitation and hygiene or workers, medical services, machinery and equipments, batch manufacturing records, distribution records, record of market complaints, quality control and the requirements for sterile products viz., manufacturing areas, precautions against contamination and mix. It also provided the list of recommended machinery, equipment and minimum manufacturing spaces required for the manufacture of various categories of ayurvedic, siddha and unani system of medicine and also in-house quality control section.

HEAVY METAL CONTENTS

Heavy metal contamination may be a particular problem with traditional remedies from India, which are currently becoming prevalent in the USA, Australia, Europe and other countries. Due to unsatisfactory Agricultural and cultivation practices relating to the medicinal plants used in preparation of Ayurveda, Siddha & Unani (ASU) and general environmental pollution, the presence of heavy metals above the permissible limit therein cannot be ruled out in the herbal preparations (Ramachandran, 2006). Strictly speaking, heavy metals are not contaminants of such drugs but are seen as active ingredients by proponents of traditional Indian medicine (Ernst, 2002). The Indian government introduced regulations in October 2005 with regard to heavy metal content in Ayurvedic formulations. Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH), in an order made testing for heavy metals namely, Arsenic, Lead, Mercury and Cadmium mandatory for export purposes in respect of every batch of purely herbal ASU drugs by every licensee. Permissible limits for Arsenic, Lead and Cadmium will be as recommended by WHO publication "Quality Control Methods for Medicinal Plants & Materials". In case of Mercury, the permissible limit will be one ppm. Conspicuous display on the container of purely herbal ASU drugs to be exported the words "Heavy metals within permissible limits" will be mandatory.

GOOD MANUFACTURING PRACTICES

AYUSH directs all the State Drug Licensing Authorities to take action against the defaulting ASU drug manufacturers for revocation of their licenses under Rules 157, 158 and 159 of the Drugs & Cosmetics Rules, 1945 for failure to comply with the Good Manufacturing Practices notified under Schedule 'T' of the Drugs & Cosmetics Rules, 1945. AYUSH directs the State Licensing Authorities of ASU drugs to ensure full compliance by all ASU drug manufacturers of the provisions of Rule 161 (1) and (2) relating to displaying on the label of the container or package of an Ayurveda, Siddha and Unani drug, the true list of all the ingredients (official and botanical names) used in the manufacture of the preparation together with the quantity of each of the ingredients incorporated therein. In case all the ingredients cannot be mentioned on the label because of their large number the same shall be indicated in the leaflet to be inserted in the package. Further that the container of a medicine shall conspicuously display the words 'Caution to be taken under medical supervision' if the list of ingredients contains a

substance specified in Schedule E(1) of the Drugs and Cosmetics Rules, 1945.

NATIONAL MEDICINAL PLANTS BOARD

Government of India decided to establish an independent body called "National Medicinal Plants Board" under the chairpersonship of ministry of health and family welfare. Its objectives are to assess the demand/supply, policy matters, guidance, inventorization, promotion of conservation or cultivation, promotion of co-operative efforts dissemination of information, matters relating to import or export, value addition, research and development, agro technology development and IPR related issues etc. The main objective of establishing the Board is to have an agency at National level which would be responsible to co-ordinate all matters relating to development of medicinal plants including drawing up policies and strategies for conservation, proper harvesting, cost-effective cultivation and marketing etc. of raw material in order to protect, sustain and develop this sector (Anonymous, 2002a). To achieve these objectives 27 state medicinal plants boards were established. The National Medicinal Plants Board has been setup as a follow-up of recommendations of the Task Force on conservation and sustainable utilization of medicinal plants by Planning Commission, vide Cabinet Resolution notified on 24th November, 2000.

PHARMACOPOEIA COMMITTEES

Laying down the Pharmacopoeial standards for Ayurveda, Siddha and Unani medicine both for single and compound drugs is an essential item of work. The Indian ministry had taken up the task of developing pharmacopoeial standards through Pharmacopoeia Committees viz Ayurvedic Pharmacopoeia Committee (APC), Unani Pharmacopoeia Committee (UPC), Siddha Pharmacopoeia Committee (SPC) and Homoeopathic Pharmacopoeia Committee (HPC). They work for preparing official formularies/pharmacopoeias to evolve uniform standards in preparation of drugs of Ayurveda, Siddha, Unani and Homoeopathy and to prescribe working standards for single drugs as well as compound formulations.

TRADITIONAL KNOWLEDGE DIGITAL LIBRARY (TKDL)

Since time immemorial, India has a rich traditional knowledge. Documentation of this existing knowledge, available in public domain, on various traditional systems of medicine has become imperative to safeguard the sovereignty of this traditional knowledge and to protect them from being misused in patenting on non-patentable inventions. The TKDL is an original proprietary database, which is fully protected under national and international laws of Intellectual Property Rights. TKDL, based on a novel way of decodification software, allows automatic conversion of information from Sanskrit into various languages. The information includes names of plants, Ayurvedic description of diseases under their modern names and therapeutic formulations, etc. During the current year, approximately 65,000 formulations will be taken up from 45 selected Ayurvedic books, out of which 23,000 will be transcribed after excluding the duplicate references. The activity on identification of the formulations has been initiated. So far more than 34000 formulations have been identified from the Ayurveda texts and they have been checked for the duplicates. Transcription of 25000 formulations has been completed from 14 texts out of the targeted 45 texts. A similar work is also being carried out in other Indian system of Medicines.

The Indian government has also established 10 new drug testing laboratories for Indian systems of medicine and is upgrading existing laboratories to provide high quality evidence to licensing authorities of the safety and quality of herbal medicines. This replaces an *ad hoc* system of testing that was considered unreliable. These laboratories are also involved in the preparation of drug formulation and pharmacopoeias for Ayurveda, siddha, Unani and Homoeopathy drugs and also in imparting training to ISM drug industry and drug inspecting staff on standardization and quality control (Mukherjee et al., 1998, 2005a). Randomized controlled clinical trials of selected prescriptions for Indian systems of medicine also have been initiated. These will document the safety and efficacy of the prescriptions and provide the basis for their inter- national licensure as medicines rather than simply as food supplements (Bodeker, 2001).

THE INDIAN MEDICINES DEVELOPMENT CORPORATION BILL, 2005

In the ancient times, India has been the leader in the medicines. Several systems, mostly indigenous, were used to cure diseases. Many herbal plants were used for manufacture of medicines. Later allopathy system of medicine came into being. Allopathy system being mostly of chemicals has its own effects while temporarily curing diseases. While Indian system of medicine provides permanent relief, allopathy system provides only temporary relief. Moreover, allopathy system has its own side effects which spoil the body system. Further the system is costlier also and poor people cannot afford to use this system. India has immense resources of herbal plants. They have not been properly explored and exploited. Moreover, there is a huge potential for export of Indian system of medicines. Therefore, it is proposed to establish a Corporation exclusively to promote and develop Indian system of medicines (Anonymous, 2005a).

The Corporation shall perform the following functions:

i. To identify and locate herbal plants which are necessary for manufacture of medicine;
ii. To protect herbal plants area;
iii. To manufacture and process Indian system of medicine;
iv. To distribute and set up outlets for selling Indian system of medicine;
v. To extend financial and technical assistance to persons involved in research in Indian system of medicine;
vi. To export medicines based on Indian system; and
vii. To advocate the extensive use of Indian system of medicine.

TRADITIONAL HERBAL MEDICINES ACT, 2006

The market in the urban and semi-urban area in India is full of traditional herbal preparations. These medicines claim to cure various ailments from general fatigue to diabetes to cancer. According to a report, a causal and random checking and testing of these medicines by the Department of Pharmacology of one of the premium referral hospitals in India revealed that many of them were contaminated containing steroids which in the long run could lead to suppression of immune system, growth retardation in children, diabetes and cataracts. Under the pretext of ancient texts and without any legal requirement of any license to sell these medicines, these unchecked traditional medicines are causing serious ailments to their innocent users. The traditional herbal medicines act, 2006 was introduced in the Indian Parliament in May, 2006 to regulate the sale of the traditional herbal medicines which are being marketed without any license and control under the cover of being manufactured by formulation provided in the ancient texts and to provide for compulsory listing and verification of ingredients of traditional herbal medicines and for matters connected therewith and incidental thereto (Anonymous, 2006c).

The functions of the Authorities are:

(i) To ensure quality control of the traditional herbal medicines.
(ii) To arrange to verify the ingredient of any medicine.
(iii) To act on the complaint received in respect of any medicine.
(iv) To recommend cancellation of license for selling of any traditional herbal medicine.
(v) To make the people aware about its findings of various spurious medicines.
(vi) To conduct survey and inspection and random sample checking of every manufacturer at least once in a year through its laboratories.
(vii) Any other function that may be assigned.

According to the act no traditional herbal medicine shall be sold or made available over the counter, every retailer or seller of traditional herbal medicines shall have to obtain a license to sell traditional herbal medicines from the Authority in such manner as may be prescribed. Every manufacturer of traditional herbal medicine shall list the ingredients of each medicine on the packing of the medicine along with their accurate quantity. Every manufacturer of traditional herbal medicine shall clearly and boldly indicate on the packaging of the medicine any side effects and warning of contraindications in such manner as may be prescribed.

CONCLUSION

The market for medicinal plants is difficult to obtain as there is no clear distinction between medicines, food, spices and aromatic usage of these plants. Facing a multi-billion dollar international trade of herbal medicines, many countries in Asia are positioning themselves to boost their share of this

business and implement appropriate regulatory measures to safeguard public health. To maximize the utilizations of the natural resources, there should be an international co-ordination leading to harmonization on various regulations of different countries. With this international harmonization, the botanicals should be explored further in the context of modern development.

Most of the herbal medicines in the world originate from developing countries, although the export volumes from most of these countries are small. There are ample opportunities for these countries to expand their global export. The Indian government has drawn up regulations for good manufacturing practice for traditional Indian systems of medicine such as ayurveda, siddha, and unani, so that the industry can compete in international markets. Government of India has taken various initiatives to improve the herbal drug standards and promote Indian system of medicine. Government of India has been stiffening the herbal drug regulations from time to time by establishing various bodies to control the manufacture and sales of herbal drug. It is continuously taking various corrective measures by implementing certain acts and rules coping with the developing global standards for natural products.

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Laboratorio Regional Latinoamericano sobre Medicina Tradicional

Entre el 10 y 12 de Mayo pasado se realizó en la ciudad de Leticia, Colombia el Laboratorio Regional Latinoamericano sobre Medicina Tradicional "Diálogo de saberes: plantas medicinales, salud y cosmovisiones. Experiencias de medicina tradicional al servicio de la salud pública", Este evento fue organizado por AIFO, Monserrate, Cooperazione Italiana, COE, MLAL Progettomondo, Universidad de Los Andes y Universidad Nacional de Colombia – Sede Leticia. Contó con la organización y sacrificio que bien valieron la pena de Enrico Neri, quien encabezó el evento. Contó con la participación de destacados investigadores internacionales: Armando Herrera (México) y Miguel Angel Gutiérrez (México), Elaine Elisabetsky (Brasil), Elena Li (Perú), Jorge Alonso (Argentina) y José Luis Martínez (Chile). Además de varios investigadores de Colombia y también muchos grupos étnicos. El logo del evento y algunas fotos se muestran a continuación:

Ldo. José L. Martinez
Editor Jefe de BLACPMA

Foto 1: Parte de los participantes posan para la foto oficial.

Foto 2: El Editor Jefe de BLACPMA junto a Enrico Neri.

Foto 3: Invitados junto a Enrico Neri, de izquierda a derecha: Enrico Neri, Miguel Angel Gutiérrez, Elena Li, José Luis Martínez, Jorge Alonso, Elaine Elisabetsky y Harold Gomez.

Foto 4 José Luis Martínez junto a Humberto Andoque, cacique y jefe máximo de la Comunidad Andoque.

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Canto IX

Desde allí dañosos vientos lleváronme nueve días por el ponto, abundante en peces, y al décimo arribamos a la tierra de los lotófagos, que se alimentan con un florido manjar. Saltamos en tierra, hicimos aguada, y pronto los compañeros empezaron a comer junto a las veleras naves.

Y después que hubimos gustado los alimentos y la bebida, envié algunos compañeros -dos varones a quienes escogí e hice acompañar por un tercero que fue un heraldo- para que averiguaran cuáles hombres comían el pan en aquella tierra. Fuéronse pronto y juntáronse con los lotófagos, que no tramaron ciertamente la perdición de nuestros amigos; pero les dieron a comer loto, y cuantos probaron este fruto, dulce como la miel, ya no querían llevar noticias ni volverse; antes deseaban permanecer con los lotófagos, comiendo loto, sin acordarse de volver a la patria. Mas yo los llevé por fuerza a las cóncavas naves y, aunque lloraban, los arrastré e hice atar debajo de los bancos. Y mandé que los restantes fieles compañeros entrasen luego en las veloces embarcaciones: no fuera que alguno comiese loto y no pensara en la vuelta. Hiciéronlo en seguida y, sentándose por orden en los bancos, comenzaron a batir con los remos el espumoso mar.

Homero, La Odisea. Canto IX
(TRADUCCION DE LUIS SEGALA Y ESTALELLA)
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