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# Search of new Antimitotics compounds from the Cuban flora

[Búsqueda de nuevos compuestos con actividad antimitótica en la flora cubana]

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**Abstract**
The main objective of anti-carcinogenic chemotherapy is to stop uncontrolled cellular proliferation. This has prompted us to begin a systematic survey of new effective inhibitors with ability to react with cytoskeletal components and arrest living, dividing cells. Even for traditional populations herbs-consuming, encouraging the use of species with chemopreventive actions could be helpful as part of life expectancy improvement strategies. Herbal products have significantly lower costs, exhibit little or no toxicity during long-term oral administration and are relatively available at large scale. Current work involved the screening of 85 extracts from Cuban medicinal plants, selected on the basis of traditional use, ethnobotanics and pharmacological information (antiparasitic, antitumour, abortive, etc.). Antitubulinic activity in the hydroalcoholics extracts was evaluated by using a modified version of the conventional turbidity assay of tubulin assembly/ disassembly. The activity limits of the news isolated antitubulin agents were thoroughly investigated. According to the presented results, the extracts displaying the highest antitubulinic activity were *Tamarindus indica L*., *Lawsonia inermes L* and *Xanthium strumarium L.*

**Keywords:** Antimitotic; Antitubulin assembly; herbal products; Microtubule; plant extract

**Resumen**
Detener la proliferación celular es el principal propósito de la quimioterapia anticarcinogénica. Para ello se ha realizado una búsqueda a partir de fuentes naturales de nuevos inhibidores efectivos que reaccionen con los componentes del citoesqueleto y puedan detener la división celular. En poblaciones que tradicionalmente utilizan plantas medicinales se estimula el uso de aquellas especies con acción quimiopreventivas como parte de una estrategia que contribuya a la calidad de vida. Los productos herbarios tienen costos significativamente más bajos, exhiben poca o ninguna toxicidad durante la administración oral a largo plazo y están al alcance de todos. Nuestro trabajo consistió en realizar un tamizaje de 85 extractos de plantas medicinales cubanas seleccionadas en base al uso tradicional, en las encuestas etnobotánicas e información farmacológica (actividad antiparasitaria, antitumoral, abortiva, etc). La actividad antitubulínica fue evaluada mediante una versión modificada del ensayo turbimétrico del ensamblaje/desensamblaje de la tubulina. Se determinó la actividad límite de los nuevos agentes antitubulínicos siendo los extractos de Tamarindus indica L., Lawsonia inermes L and Xanthium strumarium L. los de mejor actividad antitubulínica según las condiciones ensayadas.

**Palabras Clave**: antimitótico, antitubulínico, extracto de plantas, microtúbulos, productos herbarios

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## INTRODUCTION

Cancer is believed to become the main cause of death in worldwide (Eckhardt, 2002, Wilmer et al. 2007). Even when the current antitumoral therapeutic strategy comprises multiple points of intervention, cytotoxic drugs remain a mainstay in cancer chemotherapy for the next future (De flora et al.2001, Irie et al. 2004, , Fonrose et al. 2007). Antimitotic agents constitute a major class of cytotoxic drugs, and among them are included plant-derived compounds such as paclitaxel, vincristine, and combretastatin (Iwasaki, 1993). Over the last decade, several novel highly microtubule-active natural products such as epothilone, eleutherobin, and sarcodictyn have been described whose therapeutical potential for anti-cancer treatments are already tested or will be tested very soon in clinical trials (Newman et al.2001, Edelman, 2006, Groth-Pedersen et al. 2007). Due to the great number of still non-treatable kinds of cancer and to the serious side effects of these drugs and their tendency to produce resistances during anti-cancer treatment, we are faced with a current need to find new compounds and new lead structures for cancer chemotherapeutical purposes (Dozier et al.2003). Major problems of anti-cancer compounds acting on the cell-functionally obligate microtubule cytoskeleton and its main protein, the tubulin, are drug resistance formation that limits effectiveness and side effects like mutagenicity (Iwasaki, 1993, Newman et al.2001, Edelman, 2006, Groth-Pedersen et al. 2007, Dozier et al.2003, Jordan et al. 1998). A basic aim of current research is to find new highly efficient antimitotic drugs targeted to tubulin binding site different from those used by conventional drugs (e.g. paclitaxel, vincristine, or colchicine), and at the same time, able to modulate microtubule dynamics (both assembly / disassemly dynamics and dynamic instability). An intelligent search for new compounds and lead structures for microtubule-based cancerostatics would include sources such as marine organisms or medicinal plants with antiproliferative effects, known or assumed by traditional biomedicine interventions. Cuba has a vast flora and popular tradition in the use of the green medicine for the prevention and cure of various illnesses, nevertheless, its medicinal flora has been little investigated as source of compound able to inhibit the formation of microtubuls of the mitotic spindle. In current study, it is presented an screening for antimitotic activity comprising 85 hydroalcoholic extracts from Cuban flora, traditionally used as herbal remedies.

## MATERIALS AND METHODS

### *Plant Material*

The plant material was collected in Pinar del Río and La Habana provinces and properly identified at the Medicinal Plants Experimental Station "Dr Juan Tomás Roig" in Güira de Melena, La Habana.

Those medicinal plants are traditionally used by native Cuban people due to their therapeutic effects. The species are alphabetically listed in Table 1, indicating the parts of the studied plants. A voucher specimen in each case (also indicated in the table) was deposited at the herbarium of this institution.

For plant selection, two criteria were followed: results of ethnobotanics surveys and literature surveys for antiparasitic, antifungic, abortive, antitumoral or systemic toxicity activity (Roig, 1974, Fuentes & Expósito, 1995, Fuentes, 1996).

### *Extracts preparation*.

The collected species were dried and 1 Kg of dried drug was subjected to hydroalcoholic and aqueuos extracts (Martin & Cook, 1961), yielding 1l of extracts. It was concentred under reduced pressure to obtain a raw extract, kept in sealed containers at 4°C. (Soler et al., 1972). A total of 85 extracts were prepared, and their antitubulinic activity was evaluated.

### *Antitubulinic testing*

Antitubulinic activity was evaluated with a slightly modified version of the turbidity assay described by Gaskin *et al*., 1974. In this *ex vivo* assay, the assembly of microtubule protein isolated from porcine brain is monitored in presence of effectors. The modifications are: that to exclude protein denaturation and to check reversibility of assembly, the measurement was extended for additional 20 min, while temperature decreased to 4 °C. The measurements were performed at 360 nm with a UV spectrophotometer equipped with a multicell holder connected to a thermostat. For a promissory activity the absorption range was set to: 0.020 - 0.050, for a moderate activity: 0.050 - 0.080, and without activity: 0.080 - 0.100.

Out of the extracts with promissory activity those producing the lower absorption (the optic density (OD) $\leq$ 0.040) were diluted to concentrations below 1 mg/ml in order to determine its activity limits. Limit of full activity was defined as the minimal concentration of the extract displaying the highest inhibitory effect on the assembling of the tubulin, compared to the decrease of the OD.

**RESULTS**

The most general aspects of our survey about the inhibitory potential of tubulin assembly in medicinal Cuban flora are shown in table 2. Because, in some cases (*Xanthium strumarium* L., *Tamarindus indica* L., *Ricinus communis* L., *Aloe vera* L. and *Rhizophora mangle* L.), extracts from different parts of the same vegetable were obtained, the total numbers of tested extracts was superior to that of the botanical species included in the screening. Additionally from *Plectranthus amboinicus* (Lour) Spreng, hydroalcoholic and aqueous extracts were tested.

Asteraceae, Lamiaceae, Rhyzophoraceae and Rutaceae botanical families were represented in both categories of antitubulinic activity. Likewise the species *Rhizophora mangle* L was included in both categories. Their bark extract showed promissory activity while the activity of its leaves extract was moderate.

In accordance with the range of absorption, the three distinguished main categories of antitubulinic activity (- : without activity; +: moderate; ++: promissory) displayed its typical effect-curves (Figure 1).

Table 1: Tubulin assemblibility results for all plant extract tested

| No | Family | Scientific Name | Voucher ID ( No. herbarium) | Parts used | Anti-tubulinic activity [a] |
|---|---|---|---|---|---|
| 1 | *Acanthaceae* | *Justicia pectoralis Jacq. var Pectoralis* | ROIG 4636 | Aerial parts | - |
| 2 | *Amaryllidaceae* | *Pancreatum areniclum (Nothrop) Alain.* | ROIG 4660 | Rhizome | - |
| 3 | *Anacardiaceae* | *Spondias purpurea L.* | ROIG 4661 | Branches | ++ |
| 4 | *Annonaceae* | *Annona muricata L.* | ROIG 4662 | Leaves | ++ |
| 5 | *Annonaceae* | *Annona reticulata L.* | ROIG 5663 | Aerial parts | - |
| 6 | *Apiaceae* | *Anethum graveolens L.* | ROIG 4644 | Seed | - |
| 7 | *Apiaceae* | *Foeniculum vulgare Mill.* | ROIG 4623 | Branches | ++ |
| 8 | *Apocynaceae* | *Nerium oleander L.* | ROIG 4665 | Aerial parts | - |
| 9 | *Apocynaceae* | *Panicetum mutata L.* | ROIG 4730 | Branches | ++ |
| 10 | *Asteraceae* | *Artemisa absitium L.* | ROIG 4640 | Aerial parts | - |
| 11 | *Asteraceae* | *Biden pilosa L.* | ROIG 4598 | Aerial parts | + |
| 12 | *Asteraceae* | *Calendula officinalis L.* | ROIG 4625 | Flowers | - |
| 13 | *Asteraceae* | *Matricaria recutita L.* | ROIG 4692 | Flowers | - |
| 14 | *Asteraceae* | *Parthenium hysterophorus L.* | ROIG 4626 | Aerial parts | - |
| 15 | *Asteraceae* | *Tagetes erecta L.* | ROIG 4664 | Branches | + |
| 16 | *Asteraceae* | *Xanthium strumarium L.* | ROIG 4666 | Root | ++ |
| 17 | *Asteraceae* | *Xanthium strumarium L.* | ROIG 4666 | Branches | ++ |
| 18 | *Bignoniaceae* | *Crecentia cujete L.* | ROIG 4723 | Branches | - |
| 19 | *Bixaceae* | *Bixa orellana L.* | ROIG 4701 | Friuts | + |
| 20 | *Brassiaceae* | *Lepidium virginicum L.* | ROIG 4626 | Aerial parts | - |
| 21 | *Bromeliaceae* | *Bromelina pinguin L.* | ROIG 4667 | Leaves, fruits | - |
| 22 | *Burseraceae* | *Bursera simaruba (L.) Sarg* | ROIG 4668 | Branches | ++ |
| 23 | *Cactaeceae* | *Nopalea coccininellofera (L) Salm-Dyck.* | ROIG 4728 | Leaves | - |
| 24 | *Caesalpinaceae* | *Cassia grandis L.* | ROIG 4692 | Seed | - |
| 25 | *Caesalpinaceae* | *Tamarindus indica L.* | ROIG 4670 | *Bark* | ++ |
| 26 | *Caesalpinaceae* | *Tamarindus indica L.* | ROIG 4670 | Branches | - |
| 27 | *Cariacaceae* | *Carica papaya L.* | ROIG 4669 | Leaves | + |
| 28 | *Cecropiaceae* | *Cecropia peltata L.* | ROIG 4671 | Branches | - |
| 29 | *Chenopodiaceae* | *Teloxys ambrosioides (L.) Weber.* | ROIG 4639 | Whole plant | + |
| 30 | *Commelinaceae* | *Rhoeo Spathacea (Sw) Steam* | ROIG 4700 | Branches | ++ |

| | | | | | |
|---|---|---|---|---|---|
| 31 | *Combretaceae* | *Terminalia catappa L.* | ROIG 4677 | Leaves | ++ |
| 32 | *Cucurbitaceae* | *Momordica charantia L.* | ROIG 4694 | Aerial parts | - |
| 33 | *Cyperaceae* | *Cyperus rotundus L.* | ROIG 4688 | Whole plant | - |
| 34 | *Euphorbiaceae* | *Pedilanthus tithymaloides (L.) Poit* | ROIG 4697 | Stem | - |
| 35 | *Euphorbiaceae* | *Ricinus communis L. (ramos)* | ROIG 4713 | Branches | ++ |
| 36 | *Euphorbiaceae* | *Ricinus communis L. (raíz)* | ROIG 4713 | Root | ++ |
| 37 | *Fabaceae* | *Abrus precatorius L.* | ROIG 472 | Branches | - |
| 38 | *Fabaceae* | *Cajanus cajan (L) Huth* | ROIG 4689 | Branches | ++ |
| 39 | *Fabaceae* | *Erythrina sp.* | ROIG 4690 | Branches | ++ |
| 40 | *Lamiaceae* | *Melissa officinalis L.* | ROIG 4586 | Aerial parts | - |
| 41 | *Lamiaceae* | *Mentha spicata L.* | ROIG 4629 | Aerial parts | - |
| 42 | *Lamiaceae* | *Mentha x piperita L.* | ROIG 4590 | Aerial parts | - |
| 43 | *Lamiaceae* | *Ocimum basilicum L.* | ROIG 4638 | Aerial parts | - |
| 44 | *Lamiaceae* | *Ocimum gratissimum L.* | ROIG 4652 | Aerial parts | - |
| 45 | *Lamiaceae* | *Ocimum tenuiflorum L.* | ROIG 4675 | Aerial parts | - |
| 46 | *Lamiaceae* | *Orthosiphon aristatus (Blume) Miq.* | ROIG 4597 | Branches | - |
| 47 | *Lamiaceae* | *Plectranthus amboinicus (Lour) Spreng.* | ROIG 4579 | Leaves | ++ |
| 48 | *Lamiaceae* | *Plectranthus amboinicus (Lour) Spreng.* | ROIG 4579 | Leaves [b] | ++ |
| 49 | *Lamiaceae* | *Salvia officinalis L.* | ROIG 4672 | Branches | + |
| 50 | *Liliaceae* | *Aloe vera L.* | ROIG 4591 | Leaves | - |
| 51 | *Liliaceae* | *Aloe vera L.* | ROIG 4591 | Bark of leaves | - |
| *52* | *Lythraceae* | *Lawsonia inermis L.* | ROIG 4676 | Branches | ++ |
| 53 | *Meliaceae* | *Melia azederach L.* | ROIG 4687 | Aerial parts | - |
| 54 | *Musaceae* | *Musa paradisiaca L.* | ROIG 4695 | Juice | - |
| *55* | *Myrtaceae* | *Pimienta dioica (L.) Merr.* | ROIG 4609 | Aerial parts | ++ |
| *56* | *Myrtaceae* | *Psidium guajava L.* | ROIG 4727 | Leaves | ++ |
| 57 | *Nyctaginaceae* | *Boerhavia erecta L.* | ROIG 4642 | *Aerial parts* | - |
| *58* | *Pinaceae* | *Thuja occidentalis L.* | ROIG 4632 | Aerial parts | ++ |
| *59* | *Piperaceae* | *Piper aduncum L. s.l.* | ROIG 4679 | Whole plant | + |
| 60 | *Piperaceae* | *Piper auritum H.B.K.* | ROIG 4622 | Branches | - |
| 61 | *Plantaginaceae* | *Plantago major L.* | ROIG 4589 | Aerial parts | - |
| 62 | *Plantaginaceae* | *Plantago lanceolata* | ROIG 4588 | Branches | - |
| 63 | *Phytolacaceae* | *Petiveria alliacea L.* | ROIG 4678 | Whole plant | - |
| *64* | *Poaceae* | *Cymbopongon citratus (DC) Staf.* | ROIG 4634 | Branches | + |
| 65 | *Poaceae* | *Cymbopongo winterinus L.* | ROIG 4722 | Branches | - |
| *66* | *Poaceae* | *Zea mays L.* | ROIG 4686 | Estromas | + |
| 67 | *Portulacaceae* | *Portulaca oleracea L.* | ROIG 4685 | Whole plant | - |
| 68 | *Punicaceae* | *Punica granatum L.* | ROIG 4681 | Fruits | ++ |
| 69 | *Rhyzophoraceae* | *Rhizophora mangle L. (hoja)* | ROIG 4680 | Leaves | + |
| 70 | *Rhyzophoraceae* | *Rhizophora mangle L. (corteza)* | ROIG 4680 | Bark | ++ |
| 71 | *Rubeaceae* | *Coffea arabica L* | ROIG 4724 | Fruits | ++ |
| 72 | *Rubiaceae* | *Ixora coccinea L.* | ROIG 4729 | Branches | ++ |
| 73 | *Rutaceae* | *Citrus radiculata L.* | ROIG 4726 | Branches | ++ |
| 74 | *Rutaceae* | *Ruta chapelensis L.* | ROIG 4673 | Branches | - |
| 75 | *Rutaceae* | *Ruta graveolens L.* | ROIG 4630 | Aerial parts | + |
| 76 | *Sapotaceae* | *Pouteria mammosa (L.) Cronquist* | ROIG 4683 | Fruit, seed | - |
| 77 | *Solanaceae* | *Brugmansia candida Pers.* | ROIG 4691 | Leaves,flowers | + |
| 78 | *Solanaceae* | *Capsicum frutescens L. var frutescens* | ROIG 4650 | Fruit | - |
| 79 | *Solanaceae* | *Solanum americanum L.* | ROIG 4653 | Branches | - |

| | | | | | |
|---|---|---|---|---|---|
| 80 | *Verbenaceae* | *Lantana camara L. var. Camara* | ROIG 4725 | Branches | ++ |
| 81 | *Verbenaceae* | *Lipia alba (Millsp) N.E. Br* | ROIG 4611 | Aerial parts | - |
| 82 | *Verbenaceae* | *Stachitarpheta jamaicensis Valh (L.).* | ROIG 4641 | Aerial parts | - |
| 83 | Vitaceae | *Cissus sicycoides L.* | ROIG 4702 | Branches | + |
| 84 | *Urticaceae* | *Urera baccifera (L) Gaud* | ROIG 4682 | Branches | ++ |
| 85 | *Zingiberaceae* | *Curcuma longa L.* | ROIG 4693 | Rhizome | - |

[a]:The plants marked with (-/+/++ ) show no/moderate/good inhibitory activity against the polymerization of tubulin with 1 mg/mL extract concentration.
[b]: Aqueous extract

Table 2: General results of the screening

| | Botanic family | Vegetable species | Tested extracts |
|---|---|---|---|
| General Data | 47 | 79 | 85 |
| Data of Antitubulinic Activity | 21 | 36 | 40 |
| Promissory Antitubulinic Activity | 15 [a] | 24 [b] | 27 |
| Moderate Antitubulinic Activity | 10 | 13 | 13 |

a: Four of these are also included in the category with moderate activity
b: One of these is also included in the category with moderate activity

***Influence of the extracts on tubulin assemblibility***

Main results of the evaluation of the inhibitory potential of the 85 extracts against tubulin assembly are presented in table 1. Lamiaceae, with 9 species, is the broadly represented family, followed by Asteraceae, with 7 species. Fabaceae, Poaceae, Rutaceae, Solanaceae and Verbenaceae, are represented by three species in each one. In the remaining 42 families, two or a single species were included. Four of the five species that were samplering with extracts from two different parts of the vegetable manifested inhibitory activity in both types of samples. Among the 27 promissory extracts, eight were specially active, exhibiting inhibitory effect at optic density values below 0,04 OD. In order to estimate the limit of full activity in such eight extracts, dilution experiments were performed and the obtained results are presented in table 3. The hydroalcoholic extract obtained from the bark of *Tamarindus indica* L trees displayed the highest inhibitory activity in the tubulin assembly testing.

**DISCUSSION**

The medicinal flora in Cuba has 1258 species belonging to 180 families, among these, the families Asteraceae, Fabaceae, Rubiaceae, Poaceae and Euphorbiaceae are the most broadly represented ( Roig, 1974; Fuentes & Expósito, 1995.). In current screening, the 85 analyzed extracts represent to 26 % of the families of Cuban medicinal plants. According to available ethnobotanics data (Fuentes & Expósito, 1995), only 5 of the 79 species included in the screening are not of popular use. At the same time, 47 % of studied extracts corresponds to the popularly more used species.

Amount the extracts with inhibitory effects of tubulin assembly, 66,7 % displayed striking inhibitory potential (promissory activity). In brief, 45,6% of screened species (and 47% of analyzed samples) showed antitubulinic activity.

For the extracts with moderate activity, the changes in the optic density were in the range among 0,05 and 0,08, with a marked turbidity, demonstrating the microtubule presence due to the assembling of tubulin. On the other hands while the extracts with a promissory antitubulinic activity showed the decrease of absorption that evidences the inhibition of dimers tubulin assembling *ex vivo* affecting the dynamics of the microtubules and this way the formation of the mitotic spindle.

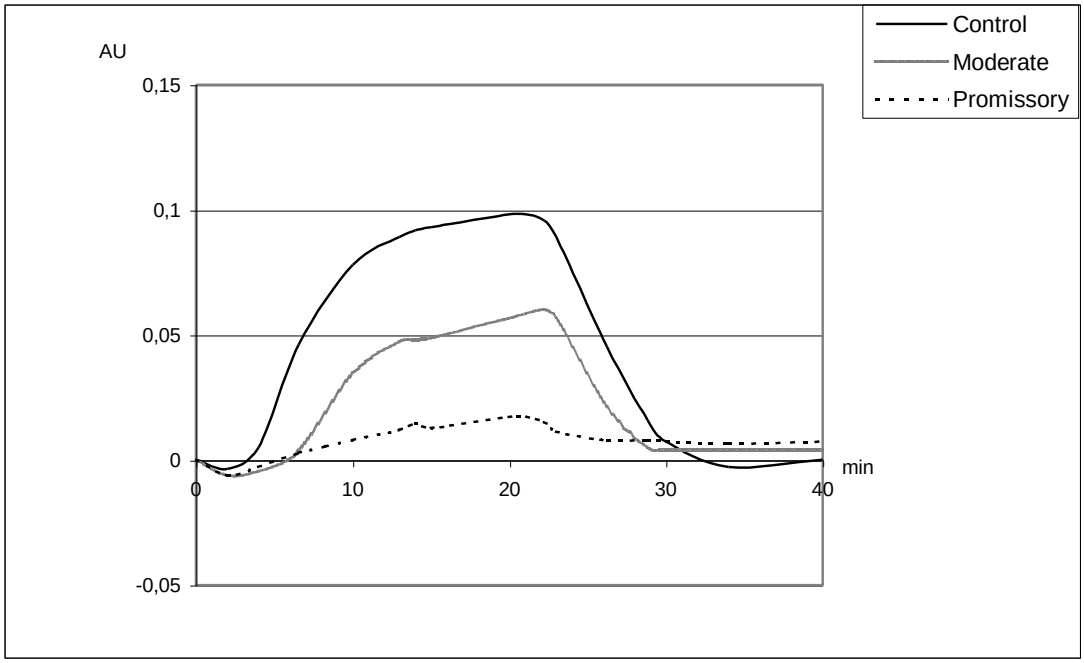
Among the 27 extracts with promissory activity, we were determined the full limit activity of 8 of them had a marked promissory activity, also supported by a wide bibliographical report.

Table 3: Summary of concentrations from most active plant extract at limit of full activity

| Scientific Name | Common Name | Anti-tubulinic activity [a] | Limit of full activity |
|---|---|---|---|
| *Spondias purpurea L.* | Ciruela | ++ | 0.5 mg/ml |
| *Xanthium strumarium L. (branches)* | Guizazo de caballo | ++ | 0.3 mg/ml |
| *Tamarindus indica L. ( bark)* | Tamarindo | ++ | 0.08 mg/ml |
| *Cajanus cajan (L) Huth* | Gandul | ++ | 0.5 mg/ml |
| *Lawsonia inermes L.* | Reseda | ++ | 0.2 mg/ml |
| *Coffea arabica L* | Café | ++ | 0.6 mg/ml |
| *Ixora coccinea L.* | Santa Rita | ++ | 0.5 mg/ml |

[a]:The plants marked with ++ show good inhibitory activity against the polymerization of tubulin with 1 mg/mL extract concentration.

Figure 1: The typical effect-curves from the main categories of antitubulinic activity.




*T. indica L*. commonly known as tamarind has been widely used in Malaysia for various purposes. In the food industry, it has been used as a food additive. The fruit have also been reported as expectorant and

anti-inflammatory agents (Lans, 2006, Melendez et al. 2006). Bioassay-guided fractionation of the methanolic extract of *Tamarindus indica L.* fruit led to the isolation of L-(–)-di-n-butyl malate which exhibited a pronounced cytotoxic activity against sea urchin embryo cells ( Kobayaski et al. 1996).

*Lawsonia inermis L.*, commonly known as Reseda is cultivated in our country and is also known for its medicinal value. Dasgupta, Rao and Yadava, in 2003, studied the anticarcinogenic potential of *L. inermis* L. extract and revealed the "dual-acting" nature, as shown from its potential to especifically induce the phase-II enzymatic activity, and inhibit the phase I enzymatic activities. In such regard, there is a wide amount of literature supporting the use of *L. inermis* L. in the hepatoprotective response (Ahmed et al. 2000).

The specie *X strumarium* L, is an annual herb which is widely spread throughout Korea, Japan and many other countries in American and Europe. *X strumarium* L. has been frequently applied as a bitter tonic, analgesic and for the treatment of cancer and strumose disease in Traditional Chinese Medicine. Kim et all (2003) found two xanthanolide sesquiterpene lactones, 8-epi-xanthatin and 8-epi-xanthatin epoxide, isolated from the leaves of *Xanthium strumarium L.*, able to inhibit the proliferation of cultured human tumour cell, A549 ( non small cell lung), SK-OV-3 ( ovary), SK-MEL-2 (melanoma), XF498 Central nervus system) and HCT-15 ( colon) *in vitro* (Kim et al. 2003). A preliminary phitochemical screening of the whole extracts of the *X. strumarium* L. was carried out followed by partial purification of the whole extracts. This study carried out by Menon et al., (2001), demonstrated that *X. strumarium L.* may posses antimitotic components. Thus this study has shown that the extracts from *X. strumarium* L. affect the polimerization of tubulin, the subunit protein of microtubules. Luo et al (2010) carried out the first report demonstrating the cytotoxic activity of cajanol towards cancer cells in vitro. Cajanol (5-hydroxy-3-(4-hydroxy-2-methoxyphenyl)-7-methoxychroman-4-one) is an isoflavanone from Pigeonpea [*Cajanus cajan* (L.) Huth.] roots. Cajanol inhibited the growth of MCF-7 cells in a time and dose-dependent manner, arrested the cell cycle in the G2/M phase and induced apoptosis via a ROS-mediated mitochondria-dependent pathway. Western blot analysis showed that cajanol inhibited Bcl-2 expression and induced Bax expression to desintegrate the outer mitochondrial membrane and causing cytochrome c release. Mitochondrial cytochrome c release was associated with the activation of caspase-9 and caspase-3 cascade, and active-caspase-3 was involved in PARP cleavage. All of these signal transduction pathways are involved in initiating apoptosis.

*Ixora coccinea* L (Santa Rita) has terpenes that response of antitumoral and antiviral activity (Monteath et al, 2000).Intraperitoneal administration of 200 mg/kg of the active fraction (AF) of the I. coccinea flower increased the life-span of transplanted Dalton's lymphoma (DLA) and Ehrlich ascites carcinoma (EAC) tumour-bearing mice by 113 and 68%, respectively. The same active fraction showed 50% cytotoxicity to DLA, EAC and Sarcoma-180 (S-180) cells in vitro at concentrations of 18, 60 and 25 microg/ml, respectively (Latha and Panikkar, 1998).
*Spondias purpurea L. Coffea arabica L* and *Urera baccifera (L) Gaud* species were not reports of antimitotic activity in the literature.

These results demonstrate the antimitotic potential of many plants of the Cuban flora traditionally used for therapeutical purposes. Among the extracts able to inhibit the polymerization of tubulin, 8 displayed a good inhibition level, being the extracts from *Tamarindus indica L., Lawsonia inermis L. and Xanthium strumarium L.* species the most active. Novel antimitotic agent discovered in this way could arise as interesting candidates for the development of further cytostatic drugs.

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