

Revisión | Review

***Jasonia glutinosa* D.C (“Rock tea”): botanical, phytochemical and pharmacological aspects**

[*Jasonia glutinosa* D.C. (Té de roca): aspectos botánicos, químicos y farmacológicos]

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Abstract

“Rock tea” (*Jasonia glutinosa*, Asteraceae) is a species used in the traditional medicine of the Iberian Peninsula and appreciated as an herbal tea regarding digestive properties. Previous works described an essential oil rich in monoterpenes such as camphor and borneol. Other extraction procedures based on the use of organic solvents have yield sesquiterpenes (lucitone, glutinone, kudtriol y 5-epi-kudtriol) as well as quercetin and kaempferol related flavonoids. The plant and its constituents have also shown antiinflammatory, antioxidant and antiprotozoal activity through *in vitro* procedures such as PGE2 release in mouse peritoneal macrophages, DPPH reduction or growth inhibition of *Leishmania donovani*, *Trichomonas vaginalis* or *Plasmodium falciparum*. Despite the wide use of the species in certain regions of the Iberian Peninsula to treat digestive disorders, there is lack of scientific evidence according to the effects on the gastrointestinal tract.

Keywords: rock tea, *Jasonia glutinosa*, Asteraceae, traditional medicine, ethnopharmacology.

Resumen

El té de roca (*Jasonia glutinosa*, Asteraceae) es una planta utilizada en la medicina popular de la Península Ibérica y apreciada como infusión, a la que se le atribuyen propiedades sobre el aparato digestivo. Los trabajos publicados hasta el momento describen la obtención de un aceite esencial que contiene monoterpenos, fundamentalmente alcanfor y borneol. Mediante otros métodos de extracción que empleaban disolventes orgánicos se han llegado a aislar sesquiterpenos (lucinona, glutinona, kudtriol y 5-epi-kudtriol) y flavonoides derivados de quercetina y kaempferol. Hasta el momento, la planta y sus constituyentes han mostrado cierta actividad antiinflamatoria, antioxidante y antiprotozoaria mediante ensayos *in vitro* como son la disminución de la liberación de PGE2 en macrófagos peritoneales de ratón, inhibición del radical DPPH y actividad leishmanicida frente a *Leishmania donovani*, *Trichomonas vaginalis* o *Plasmodium falciparum*. A pesar del amplio uso de esta especie en determinadas regiones de la Península Ibérica para afecciones gastrointestinales, hay una falta de evidencia científica respecto a los efectos de la planta sobre el aparato digestivo.

Palabras Clave: té de roca, *Jasonia glutinosa*, Asteraceae, medicina tradicional, etnofarmacología

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INTRODUCTION

According to WHO, traditional medicine is defined as diverse health practices, approaches, knowledge and beliefs incorporating plant, animal and/or mineral based medicines, spiritual therapies, manual techniques and exercises applied singularly or in combination to maintain well-being, as well as to treat, diagnose or prevent illness (WHO, 2002). Almost 80% of the world population is still using plants to treat illnesses (Gurib-Fakim, 2006). Certain traditional healthcare systems such as Traditional Chinese Medicine as well as Ayurveda or African herbal medicine are mainly based on the use of medicinal plants and are still practised in the regions where they were originated. However, European traditional medical knowledge is in an alarming state of decline (Quave et al., 2012).

European traditional plants may still be of interest in ethnobotanical and ethnopharmacological studies and they can still be a useful tool for discovering new compounds or interesting pharmacological properties (López, 2011).

Spain and the Iberian Peninsula have been the object of several ethnobotanical studies in recent years (Calvo et al., 2011; Carrió and Vallés, 2012; Cavero et al., 2011; Cavero et al., 2012; Riga et al., 2013; Rubio-Moraga et al., 2013).

Among the most common used Spanish plants, the family Asteraceae is well known, being *Jasonia glutinosa* one of the species used in traditional medicine. *Jasonia glutinosa* is used in the Iberian Peninsula to prepare an herbal tea regarding digestive properties. Although some previous phytochemical works reveal the presence of monoterpenes, sesquiterpenes and flavonoids (Gonzalez Romero et al., 2003; Guillén and Ibargoitia, 1996; Pascual Teresa et al., 1980; Rubio et al., 1995; Sanchez-Martinez et al., 2000; Villaescusa et al., 1995), there is a gap in the pharmacological knowledge of the plant, especially about the properties reported in traditional medicine. The aim of this work is to review the botanical, phytochemical and pharmacological aspects of *Jasonia glutinosa* in order to maintain the local knowledge of European traditional medicinal plants, which is a cultural heritage of importance in human healthcare.

Botanical aspects and traditional uses

Jasonia glutinosa (L.) DC., popularly known in Spanish as “té de roca” (rock tea) and used as eupeptic, is a medicinal plant with Mediterranean

distribution that grows in southern France, Iberian Peninsula, Balearic Islands and Morocco. This species belongs to the genus *Jasonia* and to the Asteraceae family, being one of the two *Jasonia* Iberian species that can be found in Spain (Pardo de Santayana and Morales, 2004)

“Rock tea” is a species with woody roots and herbaceous stems leaving about 15-30 cm with lanceolate leaves up to 3 cm having glandular hairs that produce a resinous substance with a characteristic odor. The inflorescences are situated at the top of the stems with yellow tubular flowers (Figure 1). It is considered as an aromatic plant that grows on rocky crevices and limestone landings with an altitudinal range of between 250-1800 m. They bloom in summer from July to September. This species is more abundant in the eastern half of the Iberian Peninsula and has been located in Aragón, Catalonia, Valencia, Murcia, Mallorca, Navarra, Basque Country, La Rioja and the eastern areas of Castilla León, Madrid and Castilla La Mancha.

The genus *Jasonia* was described in the 19th century (Pardo de Santayana and Morales, 2004) and the term etymologically comes from Iaso, Greek goddess of healing, one of the five daughters of Asclepio. *Jasonia glutinosa* have had other botanical names such as *Erigerun glutinosus*, *Inula saxatilis*, *Jasonia saxatilis*, *Chiliadenus glutinosus* o *Chiliadenus saxatilis*. The Spanish popular names of the plant includes: té de roca, té de Aragón, té de Moncayo, té de Gratal, té de montaña, té de monte, té de piedra, té de sierra, té de risco y árnica. This medicinal plant is also known as “te roquer” in catalan and “harkaitzetako” in euskera (vasque language). The other species of the genus *Jasonia* that can be found in the Iberian Peninsula is *Jasonia tuberosa*, also used as digestive and whose popular names are: té de burro, té de tierra or té de glera (Pardo de Santayana and Morales, 2004).

Most of the vernacular names refer to “tea” because this plant is used as an herbal tea regarding digestive properties. The most common and used name is “té de roca” (rock tea) because this plant grows in stony grounds.

Jasonia glutinosa is a very important species within traditional medicine. In Spanish, the term tea refers to any infusion of a plant regarding digestive effects (Pardo de Santayana et al., 2005). Flowered stems of the plant must be harvested between August and September and the tea is prepared to treat

stomachache, diarrhea or dyspepsia. Ethnobotanical studies (Akerreta *et al.*, 2007) have revealed that this plant is not only used where the plants grow but it can

also be found in some traditional taverns, restaurants, pharmacies and herbal remedies shops.



Figure 1
Jasonia glutinosa (Asteraceae)

This plant is mainly used in Aragón and Navarra. In the case of Aragón, the plant is used as eupeptic, mainly in the provinces of Teruel and Huesca, and it can also be combined with other herbal remedies such as dandelion (*Taraxacum officinalis*). Other traditional uses include appendicitis, colds and respiratory diseases or as an antidepressant (Villar *et al.*, 1992).

It is also an appreciated species in Navarra with similar uses to the ones in Aragón (Cavero *et al.*, 2011). It is worthy to mention that the users of the plants have attributed stimulant properties that might have a relation with the antidepressant-like effects described in certain areas from Aragón. In the south of Navarra *Jasonia glutinosa* is substituted by *Jasonia tuberosa* regarding spasmolytic, analgesic and antiemetic properties as well (Akerreta *et al.*, 2007).

“Rock tea” is traditionally used in Catalonia to prepare a liquor called “ratafia”, which is made of brandy and herbal spices such as lemon peel, nutmeg, clove and mint (Pardo de Santayana and Morales, 2004).

Besides the internal uses, some other topical applications have been documented. For example, in the province of Murcia, the plant is macerated with alcohol to treat wounds and as an anti-rheumatic remedy for bone pain (Peris *et al.*, 2001).

It is noteworthy that *Jasonia glutinosa* has more common elements with other species such as chamomiles (*Matricaria chamomilla*) in terms of botanical, chemical and pharmacological aspects than with real tea (*Camellia sinensis*). Chamomiles are traditional Iberian species that belong to the Asteraceae family. “Rock tea” shares with that group

of plants not only the botanical family but also certain components (monoterpenes, sesquiterpenes and flavonoids) and traditional uses for the digestive system.

Phytochemical studies up to date reveal the variety of compounds found in *Jasonia glutinosa* (Gonzalez Romero *et al.*, 2003; Guillén and Ibargoitia, 1996; Pascual Teresa *et al.*, 1980; Rubio *et al.*, 1995; Sanchez-Martinez *et al.*, 2000; Villaescusa *et al.*, 1995) which may explain its wide range of uses and medicinal properties.

PHYTOCHEMICAL STUDIES

Some parameters affect the chemical composition of plant extracts, such as altitude and latitude (Figuereido *et al.*, 2008). Depending on these parameters, weather conditions will be more or less advantageous for the growth of some specific plant species and will condition the proportion of certain compounds in essential oils and plant extracts (Figuereido *et al.*, 2008).

In the phytochemical studies we have taken into account for this review, *Jasonia glutinosa* was picked in the Iberian Peninsula, in particular in Guadalajara, Spain (Gonzalez Romero *et al.*, 2003; Pascual Teresa *et al.*, 1980; Rubio *et al.*, 1995; Sanchez-Martinez *et al.*, 2000; Villaescusa *et al.*, 1995) and in Zaragoza, Spain (Guillen and Ibargoitia, 1996). All the cited authors gathered this plant in summer and chose the aerial parts of the herb to carry out extractions, mainly because these parts were traditionally used in folk medicine. It should be pointed out that most of the researchers used this herbal drug dry and powdered, with the exception of González-Romero *et al.*, 2003, where no pretreatment was specified.

Methods and solvents used to obtain natural extracts are, undoubtedly, relevant parameters that also condition their final chemical composition. In the selected works for this review, authors carried out usual techniques such as maceration at room temperature with an aqueous acetone solution (Sanchez-Martinez *et al.*, 2000), aqueous methanol solution (Rubio *et al.*, 1995; Villaescusa *et al.*, 1995), where solvent/water proportion was 30:70 and 40:60, respectively, or just pure solvents as benzene (Pascual Teresa *et al.*, 1978; Pascual Teresa *et al.*, 1980). Other authors opted for hydrodistillation for 3 or 4 hours (Guillén *et al.*, 1996; González-Romero *et al.*, 2003). Apart from hydrodistillation, Guillén *et al.* (1996) also used an ultrasound bath with pentane to obtain an

extract to compare with, while González-Romero *et al.* (2003) used direct thermal desorption too. Most of these researchers carried out exhaustive separations of the components from the extracts.

Studies about chemical composition of *Jasonia glutinosa* focused on essential oil compounds (Figure 2) (Table 1), for instance the work belonging to González-Romero *et al.* (2003) and Guillén *et al.* (1996). Camphor and borneol were the two main compounds in the essential oil in both works (Figure 2), being proportions for camphor 30 - 40% and 15-20% for borneol. In the research by Guillén *et al.* (1996), other compounds with concentrations higher than 1% were detected such as nerolidol (4.2%) and τ -cadinol (2.3%). However, González-Romero *et al.* (2003) found more components with proportions higher than 1% in the essential oil; they were β -pinene (1.5%), eucalyptol (1.1%), linalool (1.7%), bornyl formate (2.9%), terpinen-1-ol (2%), caryophyllene oxide (11.4%) and farnesol (8.6%). It is important to point out that in the study done by Guillén *et al.* (1996), 27.6 % of the whole composition represented unknown compounds, whereas in the study by Gonzalez Romero *et al.* (2003) unknown compounds were only 15%; despite the fact that in the first work more substances were identified. These quantitative and qualitative differences observed in the extracts from the two cited works could depend on two factors: the place where *Jasonia glutinosa* grew, Zaragoza (Guillen and Ibargoitia, 1996) and Guadalajara (Gonzalez Romero *et al.*, 2003), and the year when it was picked, 1996 and 2003, respectively. Being these parameters so different, the difficulty to reach a conclusion increases when talking about essential oil composition, despite the fact that the selected extraction method and the chosen herb drug were the same.

Both works also compared their essential oil to another extract obtained with other methods: ultrasounds bath with pentane (Guillén and Ibargoitia, 1996) and direct thermal desorption (González-Romero *et al.*, 2003).

Proportions of oxygenated monoterpenes and oxygenated sesquiterpenes were very similar in both the essential oil and the pentane extract obtained with ultrasounds. Nevertheless, more non-polar compounds or acyclic compounds seem to be more easily extracted with the ultrasound bath (Guillén and Ibargoitia, 1996).

On the other hand, direct thermal desorption would not be the most appropriate technique to extract

essential or volatile oils, as demonstrated in the work carried out by González-Romero et al. (2003). In this paper, not only 81% of the chemical composition was unknown, but also the proportion of the most abundant

compounds decreased dramatically from 31.5% to 7.4% for camphor and from 15.7% to 3.6% for borneol.

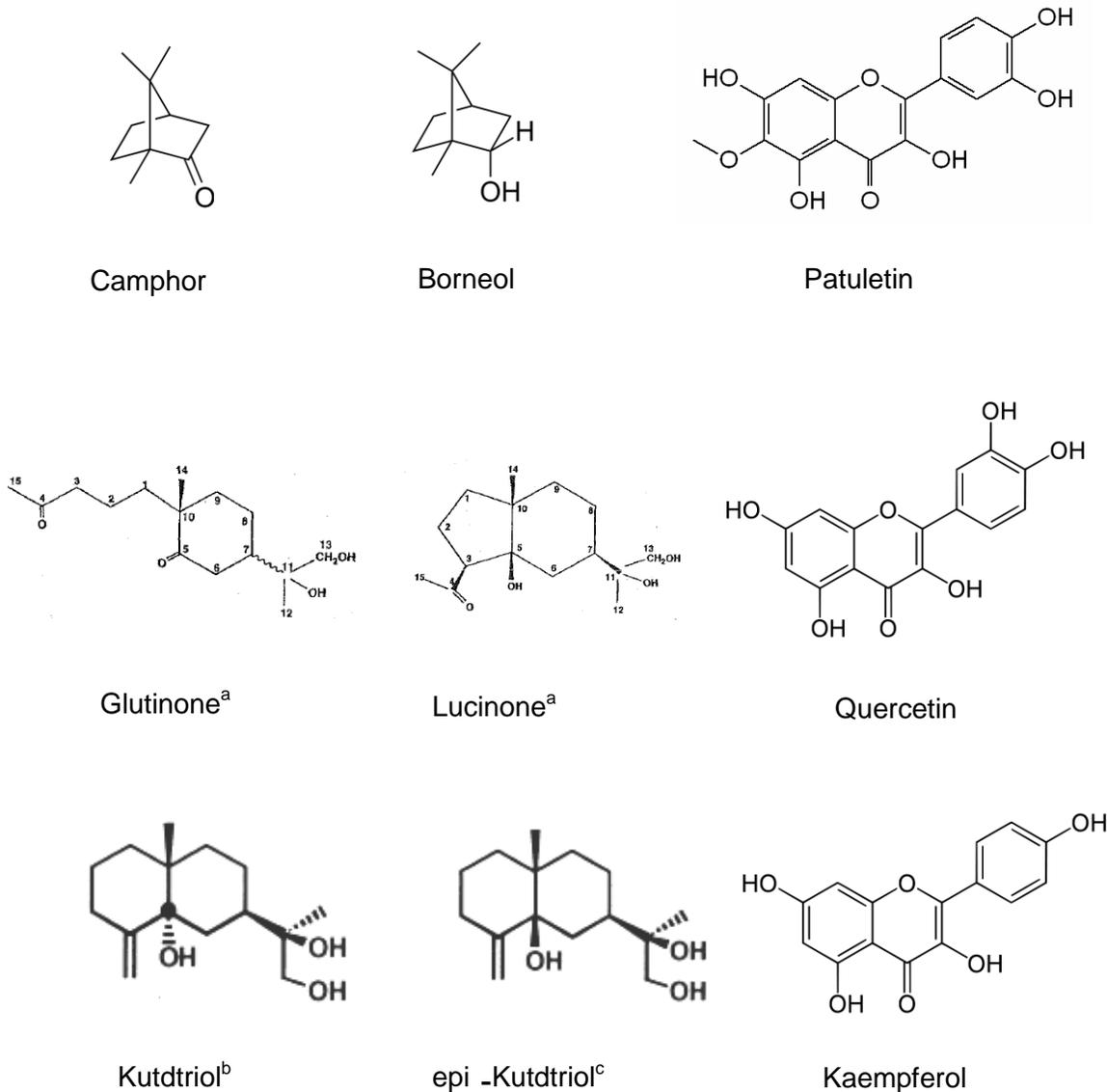


Figure 2

Chemical structure of some compounds detected in *Jasonia glutinosa*

^aVillaescusa et al., 1995; ^bPascual Teresa et al., 1980; ^cPascual Teresa et al., 1982

Apart from analyzing the essential oil and extract composition from Aragon tea, some other authors focused on identifying unknown compounds. Most of them were bicyclic oxygenated sesquiterpenes such as kudtdiol (Pascual Teresa *et al.*, 1978; Pascual Teresa *et al.*, 1980; Teresa *et al.*, 1982), α -epoxykudtdiol (Pascual Teresa *et al.*, 1980; Teresa *et al.*, 1982), (+)-costic acid (Teresa *et al.*, 1982), 5-epi-kudtdiol and kudtdiol (Pascual Teresa *et al.*, 1980; Teresa *et al.*, 1982), 12-nor-eudesm-4(14)-en-11-one (Teresa *et al.*, 1982), lucinone and glutinone (Castillo *et al.*, 1995), (11R)-eudesm-4-en-11,12-diol (11R)-

eudesmane-5 α ,11,12-triol (Sanchez-Martinez *et al.*, 2000) (Figure 2).

Others authors like Villaescusa *et al.* (1995) identified methyl flavonol glucopyranosides such as patuletin-7-O- β -D-glucopyranoside, patuletin-3-O- β -D-glucopyranoside, quercetin-3-O- β -D-glucopyranoside, quercetin-3-O- β -D-galactopyranoside and quercetin-7-O-monoglucoside, while Rubio *et al.* (1995) isolated and identified flavonol glucuronopyranosides such as kaempferol-3-O- β -D-glucuronopyranoside, quercetin-3-O- β -D-glucuronopyranoside and quercetin-3-O- β -D-glucuronopyranoside-6''-methyl ester.

Table 1
Compounds identified in *Jasonia glutinosa* and their proportions

Name	Proportion or amount			Extract fractions
	Compound proportion in essential oil (%)	Compound proportion in pentane extract with ultrasound bath (%)	Compound proportion in DTD extract (%)	
Cyclic monoterpenes				
α -pinene	tr ^a 1.5 ^b	3.5 ^a	0.3 ^b	-
Camphene	tr ^a 0.8 ^b	0.8 ^a	0.2 ^b	-
Sabinene	0 ^a	0.5 ^a	-	-
β -pinene	0 ^a 0.6 ^b	0.1 ^a	0.2 ^b	-
δ -3-carene	tr ^b	-	0 ^b	-
α -phellandrene	0 ^a tr ^b	tr ^a	tr ^b	-
α -terpinene	tr ²	tr ²		-
Limonene	0.5 ^b	-	0 ^b	-
γ -terpinene	0.3 ^b	-	0 ^b	-
p-cymene	0 ^a 0.4 ^b	0.2 ^a	tr ^b	-
Terpinolene	tr ^b	-	0 ^b	-
Cyclic oxygenated monoterpenes				
Eucalyptol or 1,8-cineol	0.1 ^a 1.1 ^b	0.2 ^a	0 ^b	-

Trans-sabinene	0.1 ^a 0 ^b	0.4 ^a	tr ^b	-
Linalool oxide	0.1 ^a 0 ^b	tr ^a	tr ^b	-
cis-sabinene hydrate	0.2 ^a	0.4 ^a	-	-
α -campholene aldehyde	0.2 ^a tr ^b	0.2 ^a	0 ^b	-
Camphor	42.4 ^a 31.5 ^b	38.3 ^a	7.4 ^b	397mg ^c
Exo-borneol	tr ^a	tr ^a	-	-
Nerol oxide	tr ^a 0.4 ^b	tr ^a	0 ^b	-
Endo-borneol or (-) borneol	17.8 ^a 15.7 ^b	12.1 ^a	3.6 ^b	230mg ^c
2-cyclohexen-1-ol	1 ^b	-	0 ^b	-
Terpinen-4-ol	0.9 ^a 0.2 ^b	0.2 ^a	0.2 ^b	-
α -terpineol	1.0 ^a	0.7 ^a	-	-
Myrtenol	tr ^a	tr ^a	-	-
Cis-piperitol	tr ^a	tr ^a	-	-
Trans-piperitol	tr ^a	0 ^a	-	-
Cis-carveol	tr ^a	0 ^a	-	-
1,7,7-trimethylbicyclo(2.2.1)heptane-2,5-dione	tr ^a	0 ^a	-	-
Campholic acid	0 ^a	tr ^a	-	-
Terpinen-1-ol	2 ^b	-	0 ^b	-
Trans-pinocarveol	0.3 ^b	-	0 ^b	-
p-menthadienol	10.7 ^b	-	0.2 ^b	-
β -damascenone	0.1 ^a tr ^b	0.1 ^a	0 ^b	-
Cis-jasmone	0.1 ^a	0 ^a	-	-
Acyclic oxygenated monoterpenes				
Linalool	0.7 ^a 1.7 ^b	0.4 ^a	0.2 ^b	-
Nerol	0.1 ^a	tr ^a	-	-
Geraniol	0.9 ^b	-	0 ^b	-

Oxygenated benzenic monoterpenes				
Benzeneacetaldehyde	tr ^a	0 ^a	-	-
4-(1-methylethyl)benzenemethanol or p-cymen-7-ol	0.1 ^a	0 ^a	-	-
Thymol	tr ^a	0 ^a	-	-
Carvacrol	tr ^a	0 ^a	-	-
Eugenol	0.1 ^a	0 ^a	-	-
1,2-dimethoxy-4-(2-propenyl)- benzene or Methyleugenol	0.1 ^a 0.8 ^b	0.1 ^a	0 ^b	-
p-cymen-8-ol	tr ^b	-	0 ^b	-
Bicyclic sesquiterpenes				
β -caryophyllene or Transcaryophyllene	tr ^a 0.8 ^b	0.5 ^a	0 ^b	-
Alloaromadendrene	tr ^a	0.1 ^a	-	-
γ -selinene	0.4 ^a 0 ^b	1.0 ^a	0.3 ^b	-
β -selinene	0.9 ^b	-	0.3 ^b	-
δ -cadinene	10.7 ^b	-	0 ^b	-
Acyclic oxygenated sesquiterpenes				
Nerolidol	4.2 ^a 0 ^b	4.6 ^a	0.1 ^b	-
Farnesol	8.6 ^b	-	0 ^b	-
Monocyclic oxygenated sesquiterpenes				
Glutinone or 2-[5'-(2'-oxopentyl)]-2-methyl- 5-(1'-hydroxy-1'- methylethanol)-cyclohexane	-	-	-	95mg ^d
Bicyclic oxygenated sesquiterpenes				
τ -cadinol	2.3 ^a	0.6 ^a	-	-
Lucinone or 5 β ,11,12-trihydroxy-iphionan- 4-one	-	-	-	59.5mg ^d

α -cyperone	0.3 ^a	0.2 ^a		-
Cariophyllene oxyde	11.4 ^b	-	2.5 ^b	-
Cadinol	0 ^b	-	1.8 ^b	-
Spathulenol	0 ^b	-	1.3 ^b	-
(+)(11R)-eudesm-4(15)-en-11,12-diol or Kudtdiol	-	-	-	17.5g ^c 17.400g ^e 0.4% ^f
(+)-(11R)-Eudesm-4-en-11, 12-diol	-	-	-	5mg ^g
(+)-(11R)-Eudesmane-5 α -11, 12-triol	-	-	-	21mg ^g
(-)-[11R]-4 α ,15-epoxieudesm-11,12-diol or α -epoxykudtdiol	-	-	-	72mg ^c 72mg ^e
(-)-[11R]-eudesm-4(15)-en-5 β ,11,12-triol or 5-epi-kudtdiol	-	-	-	119mg ^c 119mg ^e
(+)-[11R]-eudesm-4(15)-en-5 α ,11,12-triol or Kudtdiol	-	-	-	95mg ^c 95mg ^e
12-nor-eudesm-4(14)-en-11-one	-	-	-	139mg ^c
(+)-costic acid	-	-	-	300mg ^c
13-hydroxy-isocaryophylla-2(12),5-dien-7-one	-	-	-	135mg ^c
5-methoxy-caryophylla-2(12),6(13)-dien-7-one	-	-	-	120mg ^c
Cyclic monoterpene esters				
Bornyl formate	0.5 ^a 2.9 ^b	1.2 ^a	0.3 ^b	-
Endo-bornyl acetate	0.1 ^a	0.2 ^a	-	-

Other esters				
Cis-3-hexenyl tiglate	0.2 ^a	0.1 ^a	-	-
Methyl jasmonate	0.2 ^a	0.1 ^a	-	-
Alkanes				
Pentacosane	tr ^a	0.3 ^a	-	-
Heptacosane	tr ^a	0.5 ^a	-	-
Nonacosane	tr ^a	1.0 ^a	-	-
Triacontane	0 ^a	0.2 ^a	-	-
Hentriacontane	0 ^a	1.2 ^a	-	-
Dotriacontane	0 ^a	0.1 ^a	-	-
Tritriacontane	0 ^a	0.2 ^a	-	-
2-hexenal	tr ^a 0.4 ^b	0 ^a	0 ^b	-
Cis-3-hexenol or hex-3-en-1-ol	tr ^a tr ^b	0 ^a	0 ^b	-
4-hydroxy-4-methyl-2-pentanone	0 ^a	0.2 ^a	-	-
Acyclic oxygenated diterpenes				
Phytol	-	-	-	203mg ^c
Triterpenes and oxygenated triterpenes				
Squalene	0 ^a	0.2 ^a	-	195mg ^c
Dammaradienyl acetate	-	-	-	1.098mg ^c
α -amyrin	-	-	-	234mg ^c
Lactones				
Dihydrorecifeiolide	0.3 ^a	0.2 ^a	-	-
Flavonol glucuronopyranosides				
Kaempferol-3-O- β -D-glucuronopyranoside	-	-	-	16mg ^h
Quercetin-3-O- β -D-glucuronopyranoside	-	-	-	33mg ^h
Quercetin-3-O- β -D-glucuronopyranoside-6''-methyl ester	-	-	-	25mg ^h

Flavonol glucopyranosides				
Patuletin-7-O-β-D-glucopyranoside	-	-	-	22mg ⁱ
Patuletin-3-O-β-D-glucopyranoside	-	-	-	33mg ⁱ
Quercetin-3-O-β-D-glucopyranoside	-	-	-	27mg ⁱ
Quercetin-3-Oβ-D-galactopyranoside	-	-	-	24mg ⁱ
Quercetin-7-O-monoglucoside	-	-	-	8mg ⁱ
Vitamins				
α-tocopherol	-	-	-	282mg ^c
Phytosterols				
β-sitosterol	-	-	-	1.266mg ^c
Others				
Thymol related comopunds	-	-	-	432mg entre ambos derivados ^c

^aGuillén *et al.*, 1996; ^bGonzález-Romero *et al.*, 2003; ^c(no initial mass of plant is specified) Pascual Teresa *et al.*, 1982; ^d(amount referred to 1kg of dried plant) Villaescusa Castillo *et al.*, 1995^a; ^e(amount referred to 4.897kg of dried plant) Pascual Teresa *et al.*, 1980; ^f(percentage referred to dried plant mass) Pascual Teresa *et al.*, 1978; ^g(amount referred to 500g of dried plant) Sánchez-Martínez *et al.*, 2000; ^h(no initial mass of plant is specified, just the buthanolic extrac mass is given, 42.2g) Rubio *et al.*, 1995; ⁱ(amount referred to 1kg of dried plant) Villaescusa Castillo *et al.*, 1995

BIOLOGICAL AND PHARMACOLOGICAL ASPECTS

Previous pharmacological studies of the plant focused on the evaluation of anti-inflammatory, antioxidant or antiprotozoal properties.

Anti-inflammatory properties

Ciclooxigenases (COX) and lipooxigenases (LOX) are key enzymes in inflammation and considered as pharmacological targets in the search for new therapeutic compounds as they are responsible for prostaglandin, leukotriene and thromboxane formation. (Manev *et al.*, 2011).

Jasonia glutinosa contains sesquiterpenes such as lucinone, glutinone, epi-kutdtriol and kutdtriol. These compounds showed anti-inflammatory properties in a previous work with peritoneal mice

macrophages (Bermejo *et al.*, 2002). All sesquiterpenes exerted COX-1 inhibiting properties, decreasing the production of PGE2 in cells with the following IC₅₀ values: lucinone (42.69 μM), glutinone (3.61 μM), 5-epikutdtriol (1.28 μM) and kutdtriol (39 μM). These data were compared with the COX-inhibitor indomethacin (IC₅₀: 0.24 μM). However, these isolated compounds did not produce 5-LOX inhibition, obtaining leucotrienes levels (LTC4) without significant differences versus control in the experiments. This study was also carried out in human platelets measuring thromboxane B2 (TXB2) release using the calcium ionophore A23187; in this case, only glutinone (25 μM) produced a significant decrease on TXB2 release with an IC₅₀ value of 24 μM. Ibuprofen was used as a positive control substance that produced 99% of TXB2 inhibition at

100 μ M, (IC₅₀:1.27 μ M). Therefore, four sesquiterpenes isolated from *Jasonia glutinosa* exerted COX-1 inhibition but effects in 5-LOX were not observed in the cells. Anti-inflammatory effects of these molecules may be attributed to the methyl group that all have in carbon 10. Differences between kuttatriol and 5-epikuttatriol might be due to cis /trans stereochemistry in carbon 5. 5-epikuttatriol showed better activity on COX-1 inhibition than the other compounds and only glutinone showed a decrease on PGE2 and TXB2 release. The effect of this compound on TXB2 seems to have a relation with the aliphatic chain on carbon 10 (Bermejo *et al.*, 2002).

Antioxidant activity

Natural antioxidants, especially those coming from diet, have an important role in human health as they are considered molecules that exert protective effects against oxidative stress, ageing and degenerative diseases.

In relation with this, a study on antioxidant capacity of sixteen plants from Spanish traditional medicine was published in 2008. Dichloromethane, ethyl acetate, methanolic and aqueous extracts of aerial parts of *Jasonia glutinosa* demonstrated free radical scavenging effects in terms of reducing the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical. Methanolic and aqueous extracts were the most promising, with IC₅₀ values of 29.80 y 31.32 μ g/mL, being these values in the range of other synthetic antioxidants used in the study such as butylhydroxytoluene (BHT) (Lopez *et al.*, 2008).

Some compounds detected in *Jasonia glutinosa* previously demonstrated antioxidant properties in other studies involving other plant species. That is the case of the monoterpene borneol, which showed antigenotoxic effects on hepatocytes and testicular cells of rats when given orally in drinking water (Horvathova *et al.*, 2009; Horvathova *et al.*, 2012). Other authors verified that borneol reversed oxygen-glucose deprivation followed by reperfusion induced neuronal injury, nuclear condensation, intracellular reactive oxygen species (ROS) generation and mitochondrial membrane potential dissipation in cortical neurons (Liu *et al.*, 2011).

Some other plant species, for example sage (*Salvia officinalis*), share compounds with *Jasonia glutinosa* such as borneol, linalool, α -terpineol, thymol, eugenol, β -caryophyllene, farnesol and caryophyllene oxide (Sellami *et al.*, 2012). These

compounds may be in part responsible for the antioxidant and free radical scavenging activities.

Several studies have also demonstrated that flavonoids are plant secondary metabolites with antioxidant properties. For instance, kaempferol showed protective effects against endothelial damage and its mechanism may be associated with an improvement in nitric oxide production and a decrease in asymmetric dimethylarginin levels (Xiao *et al.*, 2009). Red wine polyphenolic compounds reduced infarct size and oxidative stress in a rat model of ischemia-reperfusion (Ralay Ranaivo *et al.*, 2004). Flavonoids also possess anti-inflammatory and anti-platelet aggregation effects through inhibition of relevant enzymes and signaling pathways, resulting ultimately in lower oxidant production and better re-establishment of blood in the ischemic zone (Akhlaghi and Bandy, 2009). According to previous works we can state that antioxidant properties of *Jasonia glutinosa* are also related to its flavonoid content (Rubio *et al.*, 1995; Villaescusa *et al.*, 1995).

Anti-protozoal activity

Plants are a well-known source of antimicrobial agents and in recent years, essential oils and its components have shown antibacterial, antifungal, antiviral, anthelmintic and antiprotozoal properties (Borges *et al.*, 2012). However, many of the screened plants need pharmacological and clinical studies.

There are few works on anti-parasitic effects of *Jasonia glutinosa* and they are focused on *in vitro* properties of the plant against protozoa. Villaescusa *et al.* (1996) demonstrated that acetone extracts obtained from aerial parts exerted an antiparasitic effect against *Leishmania donovani* promastigotes and *Trichomonas vaginalis* trophozoites at concentrations of 100 μ g/ml and 250 μ g/ml. However, no effect was detected against *Entamoeba histolytica*. With the aim of investigating the active compounds of the plant, Villaescusa-Castillo *et al.* (2000) evaluated the effect of the sesquiterpenes 5-epi-kuttatriol and kuttatriol on *Plasmodium falciparum* and *Leishmania donovani*. Results showed that only kuttatriol was active against both parasites at 250 μ g/ml.

Some compounds that can be found in the essential oil of *Jasonia glutinosa* such as camphor, borneol, carvacrol and eugenol showed antiparasitic activity in some other studies. For example, Ahmed *et al.* (2011) analyzed the leishmanicidal activity of 10 essential oils from Tunisian traditional plants and observed that *Thymus hirtus* sp. *algeriensis* essential

oil (13.82% camphor) had a potent activity against *Leishmania major* and *L. infantum*. Tariku et al. (2011) demonstrated that *Artemisia absinthium* essential oils (27,4% camphor) also inhibited promastigotes and amastigotes from *Leishmania aethiopica* y *L. donovani*. Eugenol was identified as an useful agent against *Giardia lamblia* (Machado et al., 2011) and carvacrol as an antimicrobial monoterpene (Nostro and Papalia, 2012) that may as well be responsible for the activity of certain essential oils against *Tripanosoma cruzi* y *Leishmania amazonensis* (Escobar et al., 2010).

Borneol was assayed on *Meloidogyne incognita*, a plant parasite of agronomic importance, demonstrating inhibition of larval motility (Echeverrigaray et al., 2009).

Although few works reveal the mechanism of action of the active compounds or extracts, it has been suggested that essential oils, for example, interact directly with biological membranes inducing changes in permeability and the death of parasites (Bakkali et al., 2008).

Other activities

López et al. (2008) verified the antifungal activity against *Rhizopus stolonifer*. This is a phytopathogenic fungus that does not affect human health. However *Rhizopus stolonifer* could be used as a model when determining the antifungal activity against filamentous fungi.

López et al. (2008) observed that only the dichloromethane extract showed activity (MIC >1000 µg/mL) and they hypothesized that sesquiterpenoids were responsible for this effect.

CONCLUSIONS

Although there are some studies verifying the effect of some isolated compounds present in *Jasonia glutinosa* on gastrointestinal tract, there is a lack of data concerning the effect of the whole extract.

A very interesting study about the activity of *Anthemis mauritiana* essential oil on jejunum smooth muscle suggests that this plant induces spasmolytic reactions due to a blocking of calcium entrance in voltage-dependent calcium channels and a blocking of calcium exit from intracellular stores. The reason for this behavior seems to be a double inhibition: on one hand this essential oil inhibits the contractile effect caused by high extracellular potassium concentrations and, on the other hand, the contraction provoked by carbacol (Karim et al., 2010). The cited effect is

associated to α -pinene, one of the identified compounds in this essential oil and in *Jasonia glutinosa* extracts.

Another research about the inhibition of ileum smooth muscle contraction when incited with acetylcholine and KCl shows that flavonoids isolated from *Rubiaceae*, such as quercetin, are responsible for this bioactivity. This effect is explained by a decrease in calcium concentration due to the block of ATP-dependent potassium and calcium channels (Cimanga et al., 2009). Finally, Attaguile et al. (2004) also suggest that the spasmolytic activity of different plants on smooth muscle is due to phenolic compounds, such as quercetin, kaempferol and methylated flavonoids. These molecules were identified and isolated in *Jasonia glutinosa* and could be responsible for the digestive properties.

Taking into account all these parallel works, where many compounds are also identified in *Jasonia glutinosa* extracts, it seems that there might be evidences for bioactivity on the gastrointestinal tract; however more studies should be carried out to verify the traditional use of this plant.

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