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Traditional use of the genus *Renealmia* and *Renealmia alpinia* (Rottb.) Maas (Zingiberaceae)–a review in the treatment of snakebites

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ABSTRACT

Renealmia alpinia (*R. alpinia*) typically occurs in the tropical rainforests of Mexico to Peru, Brazil through the Antilles, Guyana, Suriname, Colombia and Venezuela. It has traditionally been used against snakebite in Colombia. In addition to the common local use for pain, *R. alpinia* has been used as an antipyretic and antiemetic to treat wounds, malignant ulcers, epilepsy and fungal infections. The species of the Zingiberaceae family are famous for their use as spices and herbs. This review provides information on the traditional use of plants in the Zingiberaceae family, *Renealmia* genus, and specifically *R. alpinia*. We conducted a narrative review in English and Spanish in electronic databases, such as ScienceDirect, Napralert, PubMed, ScFinder, SciElo, during August 2011 to March 2013. We were interested in their applications in ethnomedicine and their chemical components, providing a major and methodical revision. We found 120 sources, 98 of which were selected as they contained essential information. This study has stimulated the development of a new work, which aims to isolate and evaluate metabolites from *R. alpinia* leads toward the development of a phytotherapeutic product, which might be accessible to the population. Studies on the toxicity and safety of *R. alpinia* are insufficient to provide information on the ethnomedical use of this species. Thus, the present review summarizes information about *R. alpinia* and proposes possible scope of future research to fill gaps identified in this narrative review.

1. Introduction

Renealmia alpinia (Rottb.) Maas (*R. alpinia*) ("matandrea" or "achira monte") has traditionally been used against snakebite by indigenous Embera–Katíos tribes belonging to the regions of Antioquia and Chocó, Colombia[1]. Poisoning by snakebite is a serious public health problem in large parts of Asia, Africa and Latin America[2–4]. Snakebites mainly affect the population living in rural areas[5]. Traditionally, it has been neglected by health authorities, research agendas, and large pharmaceutical companies in the world. Thus, the World Health Organization has added it to the list for 'neglected diseases'[6]. In recent years, there has been a renewed interest in the study and care of this problem, which has been reflected in various activities at the national, regional and global level.

The snakebite is a public health problem around the world with between 5.4 and 5.5 million people annually bitten, producing around 40 000 amputations and between 20 000 and 125 000 deaths[2,5]. In 2010, Colombia recorded 4 526 cases of snakebite accidents with an incidence of 0.82 cases per 1 million population, and a mortality rate of 0.84%[7].

The province of Antioquia is the area of the country where the majority of snakebites occurs with an incidence and a mortality of snakebites which is 9.2 and 0.14 per 100 thousand inhabitants, respectively[8]. These incidents are usually caused by *Bothrops* species[9], especially in Urabá, Cauca, Magdalena and the eastern regions of the province.

The only effective treatment for snakebite is antivenom, but in most accidents, medical intervention does not start quickly enough, mainly due to geographical factors, the limited availability of antivenoms in remote areas, and limited effectiveness of specific treatment to neutralize

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some local effects, such as hemorrhage, edema and myonecrosis, caused by the poison of vipers[10,11].

Therefore, the Ophidism/ Scorpionism Program of Antioquia's University is interested in undertaking a thorough study of *R. alpinia* to find an alternative treatment against snakebite. In 2001, it was confirmed that *R. alpinia* had anti-edema, anti-hemorrhagic and neutralizing effects on the venom of the snake *Bothrops asper* (*B. asper*) (mapaná X), both *in vitro* and *in vivo*, constituting a source of molecules with potential pharmaceutical use[1,12-14]. In order to improve the productivity and uniformity of the extracts of *R. alpinia*, our research group carried out the *in vitro* propagation of this plant species to have enough material, which through traditional cultivation could not have been achieved[15]. Subsequently, different extracts obtained with solvents of increasing polarity were studied through chromatographic fractionation in order to find the fraction responsible for the antiophidic activity. In addition, it was possible to prove in experimental animals, that *R. alpinia* possesses analgesic activity, which may contribute to relief of pain that occurs after a bite[16].

At present, it is intended to isolate and purify some secondary metabolites *R. alpinia* leaves from the extracts obtained by micropropagation and wild method, making a comparison of the chemical content and its analgesic and antiophidic properties. In order to guide these studies, we conducted a through review of this botanical species from the chemical and pharmacological viewpoint or perspective, that has been poorly studied in, for instance the genus *Renealmia*, and the results are described below.

2. *R. alpinia* (Rottb.) Maas, 1975

R. alpinia belongs to the Zingiberaceae family, characterized by having species of great pharmacological and nutritional importance, such as the ginger *Zingiber officinale* Roscoe (*Z. officinale*), the cardamom *Elettaria cardamomum* (L.) Maton, and its many ornamental purposes.

2.1. Common names and synonyms

Synonyms: *Amomum alpinia* Rottb[17].

Common names: In Colombia *R. alpinia* is popularly known by the names: "guaiporé", "matandrea" and "achira bush". Other common names in different latitudes, depending on the language are "frog eggs", "sarandango", "Abebe" (Spanish), "haimonor" (huitoto), "conoba" (Miraña), "Mubai-kurugameku "(muiname), "Huitillo"[18,19]. Table 1 lists the common names of *R. alpinia* as used in the Neotropics.

2.2. Geographical and altitudinal

R. alpinia is typically found in tropical moist lowland rainforests[22,25]. It is distributed from Mexico to Peru and Brazil through the Antilles, French Guiana, Guyana, Suriname and Venezuela. Its distribution can reach up to 1 500 m altitude[19]. In Colombia, it is located in the Antioquia and Chocó departments. Specifically in Antioquia, it has been found in the Eastern region, especially in the town of San Luis. It has also been reported to the south of the country in Caquetá, Putumayo, Guaviare and Amazon, and on the Eastern plains.

2.3. Taxonomy and botanical description

Herbaceous plant of between 2 m and 6 m high, gregarious, simple leaves, alternating, without stipules, long-lanceolate leaves up to 110 cm long and 11 cm wide, parallel rib, open leaf sheath with ligule. In addition, racemose inflorescence with basal 20-50 cm long; reddish-pink inflorescence bracts, reddish-brown rachis; tubular flower, yellow or red. Fruit in capsule, red when it is immature, black when it ripe, ovoid, 3-4 cm long and 1.5-2.0 cm in diameter, with numerous seeds embedded in a yellow pulp[18].

2.4. Popular uses

R. alpinia has traditionally been used by the Chocó indigenous tribe as an agent against the bite of *Bothrops* (mapaná X)[1]. Likewise, in traditional medicine, *R. alpinia* has been extensively used as a febrifuge (anti-fever, antipyretic) and antiemetic to treat wounds and malignant ulcers[23]. In addition, in Suriname, it is also used to treat epilepsy[30].

Furthermore *R. alpinia* is traditionally effective against fungal infections and for the preparation of oils from seeds. Furthermore, it is used as edible (aryl seed), against nausea and vomiting[30,31]. Even some parts, such as pieces of leaf sheaths, are added to the planting holes of some crops, such as corn, to avoid being eaten by rodents and birds[19].

Table 1

Common names of *R. alpinia* according to languages used in the Neotropics and its popular uses in different countries[19].

Common name (Language)	Country	Part used	Method and application	Reference
Guaiporé, Naiku (Curripaco) Pintura negra	Colombia	Leaves and stems dried rhizomes	Infusion for stomachache, Oral decoction used for snakebites	[1,20,21]
Ixquihit (nahua) X´quijit-totonaco	Puebla (Mexico)	Leaves	Repel ectoparasites from chickens and ducks	[22,23]
Mardigra	Trinidad, Tobago	Leaves	Information not found	[24]
Jazmín de monte	Guatemala	Leaves	Information not found	[25]
Mususi	Venezuela	Leaves	Information not found	[26]
Information not found	Honduras	Leaves and stems	Decoction used to clean the skin.	[27,28]
Masusa	Suriname	Dried leaves	Used as food, oral infusion used as a febrifuge, Epilepsy	[29,30]
Naiku	Brazil	Leaves and stems	Infusion for headaches	[21]

Moreover, a decoction of the stems, the whole plant, and its roots are used to treat vaginal infections and to relieve digestive ailments such as indigestion (carminative action), heartburn and stomach pain[32].

It is a valuable ornamental species due to its yellowish red inflorescences and its very bright scarlet red fruits. The macerated plant mixed with water is rubbed on the body of dogs to improve their skill in hunting[33]. Likewise, in ethno-veterinary uses, *R. alpinia* is used in Trinidad and Tobago to treat parasites coming from chickens and ducks[24], and against snakebites in dogs[34].

2.5. Pharmacological activities

R. alpinia has been poorly studied from the pharmacological standpoint. It has been shown that it has antiedematous, antihemorrhagic, and neutralizing properties of the *Bothrops atrox-asper* (mapaná X) poison[35]. Likewise, it has antimalarial and leishmanicidal activities[36]. It has been shown through citotoxity studies that *R. alpinia* rhizomes has a substantial and strong antiproliferative effect on tumor cells[37].

2.6. *R. alpinia* micropropagation

Plant propagation by *in vitro* medium is important because it is possible to have a control over the processes concerning morphogenetic, physiological and biochemical plant tissues. In addition, cultivating an explant with potential differentiation in an aseptic environment, in presence of nutrients in balanced amount, favors its development and the production of plant metabolites.

The snakebite and scorpion program at the University of Antioquia was a pioneer in the study and *in vitro* propagation of *R. alpinia*. Through this research group, it has been possible to develop some work to evaluate and compare the inhibitory capacity of ethanol extracts of leaves, rootlets, and fractions obtained by column chromatography of *R. alpinia* cultivated by *in vitro* propagation on the indirect hemolytic, proteolytic and coagulant impacts and effects induced by the venom of the snake *B. asper*.

The results obtained, show that the vemom indirect hemolytic activity is inhibited most by the fraction 7-8 [(47.30±2.20)%], followed by rootlets extracts [(32.60±6.90)%], and leaves [(24.20±4.43)%] cultured by *in vitro* propagation and leaves of *R. alpinia* cultivated in the wild [(16.20±3.88)%]. The proteolytic activity is inhibited largely by leaf extracts of the plant grown and micropropagated in the wild without significant differences. Against the coagulant activity, it has registered a greater neutralization by rootlets [(81.73±9.94) seconds]. Potential proteolytic action mechanism of *R. alpinia* on the venom of *B. asper* is unlikely since no change in the electrophoretic patterns of venom is produced[38].

2.7. Chemical composition

R. alpinia (Rottb.) Maas is characterized by its rich content of flavonoids (flavanones, chalcones) derived from the shikimic acid pathway, which have proven to be highly active biologically[39]. In a study to assess the effect of the ethanol extract and fractions obtained from *R. alpinia* on snake venom *B. asper*, the fractions show a predominant presence of coumarins[15]. Steroids, carotenoids, monoterpenes, diterpenes (labdane diterpenes), and sesquiterpenes have been found in the leaves of *R. alpinia*, many of which are yet to be elucidated or characterized[40,41]. Regarding essential oils, a large number of components in leaves, stems and fruits of *R. alpinia* have been identified.

3. Genus *Renealmia* L.f., 1781

3.1. Geographical distribution

Renealmia L.f. is one of the tropical plant genera belonging to Zingiberaceae. It is distributed throughout regions of Africa and South America[42]. It comprises about 85 species, of which 62 are in the American tropics[43]. This is the only genus native to the geotropic[44].

3.2. Botanical description

Plants of *Renealmia* are characterized by perennial and aromatic herbs. They grow up to 6 m high. The stems are numerous, clustered simple, alternate, elongated and distichous, leaves with ribbed sheaths and short or absent petiole. The inflorescence is usually a thyrsus, cluster or a pin, a terminal on a leafy stem or basal at the apex of a scape, bracts and bracteoles present in the plant. In addition, the *Renealmia* plants show flowers with colors ranging from whitish to yellow or reddish, tubular, turbinate or urceolate calyx, corolla with a labellum of 3 lobes, lateral involute lobes, reduced lateral staminodes. The fruits are in a capsule, irregularly ellipsoid, few to numerous bright brown seeds with a big, red, yellow or white aryl[44].

3.3. Popular uses

According to their chemical composition, different species of *Renealmia* are widely used for the treatment of various diseases. In Table 2 some species of this genus, the common name of the plant part used and the chemical components are described or related.

The leaves of plants in this species have various uses, such as to treat fevers resulting from snakebites. Fruits (contain the aryl of the seeds) of *R. alpina* and *Renealmia thyrsoidea* produce a blue-black ink that once boiled, and add an oil color and flavor to rice[54]. Several species are widely used as ornamentals, since their rhizomes′

Table 2

Some uses and chemical composition of species of *Renealmia*.

Species	Common name	Country	Traditional use	Part used	Chemical components identified	Reference
R. alpinia	Matandrea	Colombia, Suriname	Snakebites Food	The whole dried plant; dried leaves	Pinene, beta: monoterpene, oleorresine 22.3%. *Renealmia* diterpen. Felandreno, beta: monoterpene oleorresine 38.0% Labda-8 (17)-trans-12-dien-15-16-dial-11-15-hemiacetal, 11-hidroxiditerpen Labda-8-(17)-trans-12-dien-15-oico,16-oxo caroten, beta: carotenoids oleorresine, Labda-8-(17)-trans-12-dien-15-16. Manool: diterpen oleorresina, nerolidol: sesquiterpene oleorresine, Labda-8 (17)-trans-12-dien-15-16-diterpene oleorresina, Limonene	[29,39,40]
Renealmia chrysotricha		Brazil		Dried leaves	Aromadendrene: sesquiterpene Calamenene, cis: sesquiterpeno. Ledol: sesquiterpene. Palustrol: sesquiterpene	[45]
Renealmia cincinnata		Cameroon		Nuts	Eudesma-1-4-7-triol sesquiterpene, germacra-trans-1 (10)-trans-5-dien-4-beta-ol: sesquiterpene, germacra-trans-5-10 (14)-dien-1-beta-4-beta-diol: sesquiterpene, Oplodiol: sesquiterpeno, Oplopanone: sesquiterpene, Reneilmolsesquiterpene.	[46]
Renealmia exaltata	Masusa, mardigrass, misquipanga, pacová-catinga	Trinidad	Healing, digestive, stomach	Dried leaf and seed; rhizome	Kaempferol flavonol. Pacovatinin diterpene: flavonol quercetin, Renealtin A and B: bencenoide	[47,48]
Renealmia floribunda		Brazil Surinam	Used for vaginal baths	Essential oil from the leaf	Ethyl monoterpenes Burbonene, beta: sesquiterpene, Carveol, trans: Carnova monoterpene: monoterpene, 1,8-cineole, Myrtenal, Perilla: aldehído, Linalool, Cimeno, Limonene, Pinene, alfa y beta, Tuyona alfa.	[49]
Renealmia guianensis		French Guiana		Dried rhizome	Labda-8 (17)-12-dien-15-16: diterpene	[50]
Renealmia nicolaioides	Matandrea	Peru		Dried root	Chalcona, 2´-hidroxi-4´-6 ´-dimetoxi: flavonoids, Furan-2-carboxílico, 5-estirilo, Nicolaioidesin: benzenoid nicolaioidesin: benzenoid nicolaioides: benzenoid, Panduratin: flavonoid, Tsugafolin, flavanone, Pinostrobin: flavanone	[51]
Renealmia thyrsoidea		India, Equator	Used as an antidote in oral infusion to treat snakebites (*Bothrops atrox*)	Dried leaves	Information not found	[52,53]
Renealmia aromatica	Chucho	Honduras	Used to clean skin and inflammation	Dried leaves	Information not found	[28]

propagation can be cultivated easily.

4. Family Zingiberaceae

Zingiberaceae is the largest family in the order Zingiberales with 53 genera and over 1 200 species and is one of the leading families of tropical plants. The first family classification was proposed in 1889 and since then, it has been refined. Currently, there are four recognized tribes (Globbeae, Hedychieae, Alpinieae and Zingibereae) based on morphological characteristics, such as the number of cores and placentation in the ovary, staminodes development, changes in fertile anther, and the orientation of rhizome. The new phylogenetic analyzes based on DNA sequences suggest that some of these morphological traits are homoplasious and three tribes are paraphyletic[55].

Zingiberaceae is distributed in the Neotropics with the *Renealmia* genus. Four other genera (*Afromomum, Aulotandra, Siphonochilus* and *Renealmia*) have been identified in Africa and the rest of the genera are distributed in East Asia and the Pacific Islands. The species of the Zingiberaceae family are famous for curing ailments[56,57], also for their uses as spices and herbs. The rhizomes of several species are used as insect repellents and against snakebite[1]. Many compounds with novel structures and a large number of biologically active compounds have been identified in species of the Zingiberaceae.

From the taxonomic point of view, the family Zingiberaceae is unclear and unknown, with various genres and many species[55,58-62], which is evidence that identification and description have been carrying out for less than 20 years, making it an important object of study.

The circumscription of several genera of this family has been debated[58,63], and consensus has not been reached on the actual number of genera in the family. Almost a quarter of the genera are monospecific, but there are no criteria for the recognition of these species; these have only been established to genus level. An important issue in the classification of the family is the way to determine the taxonomic status of these monospecific genera, which are often morphologically very different[55].

4.1. Botanical description

The botanical species belonging to the Zingiberacea family are mainly grasses or herbaceous plants, provided of rhizomes with large sessile leaves having a sheath that surrounds the stem. The flowers, mostly zygomorphic hermaphrodites, gather around in inflorescences of various types and possess a perianth with distinct calyx and corolla, which consist of three elements: the androecium, originally formed by two whorls of three parts, comprising a single fertile stamen and the other stem elements are partially fused and transformed into structures of corolline aspect, the labellum and petaloidous staminodes. The gynoecium consists of 1-3 carpels soldiers in an inferior ovary. Inflorescences in the Zingiberaceae are capitated, eared, racemose or paniculate, terminal on foliar stems or basal leaf on scapes, bracteate flowers, bracts holding one or more irregular flowers, tubular turbinated calyx, usually lobed and commonly with a lateral slit or gap, tubular corolla, lobed, anther introrsa, bilocular, normally trilocular ovary. The fruit is in a capsule, the exocarp is fleshy, and the seeds are arylated, ranging from few to many, very variable in shape[64].

The structure of the flowers and their nectar favor the pollination despite of being ephemeral (lasting one day). The arylated seeds have ornitocora, mastozoocora, and mirmecocora spreading. Flowers have highly specialized mechanisms (such as the established relationship between style and stamen) in relation to pollinators for instance, insects, bees, lepidoptera and birds such as *Hornstedtia* and *Nicolaia*[65]. The fleshy and indehiscent fruits of some African species are dispersed by primates and elephants (endozoochory). *Z. officinale* (ginger), like many other species, rarely produces seed, so the vegetative propagation is more efficient and frequently used. The most notable species among Zingiberaceae are: ginger (*Z. officinale*), herbaceous plant from tropical Asia with the rhizome rich with aromatic substances, especially sesquiterpenes, used as spices, and the cardamom (*Elettaria cardamomum*) also from Asian, whose fruits are prized[64].

4.2. Distribution/ habitat

The species are highly distributed throughout India, tropical Asia and spread to northern Australia. In America the family is found in the central and southern parts of the continent. It is especially abundant and prolific in the Amazon in countries like Colombia, Peru and Brazil[59,66].

4.3. Ecology

The Zingiberaceae is a family of tropical plants, present in many of the equatorial regions of the world. The greatest concentration and diversity is in Southeast Asia, especially Indomalesia. It is mainly found in habitats below the forest canopy, shaded to semi-shaded, occasionally in wetlands or humid places[67]. The flowers of the Zingiberaceae have various colors and shapes, and are mainly pollinated by insects (bees, moths, butterflies) and birds. Many species are cross-pollinated, but also occurs self-pollination and vegetative reproduction. Some species of the genus *Globba* reproduce asexually. Birds are the most common dispersant, fleshy capsules are usually colored and often, these contrast with the brightly colored arylated seeds[65].

4.4. Taxonomy

In the Zingiberaceae, 46-52 genera and 1 075-1 300 species have been classified. The most representative genera are *Alpinia* (150 species), *Amomum* (120 species), *Zingiber* (90 species), *Renealmia* (85 species), *Globba* (70 species), *Curcuma* (60 species), *Kaempferia* (60 species) and *Hedychium* (50 species)[43].

4.5. Chemical composition of Zingiberaceae

Vegetal extracts are a rich source of pharmacologically active molecules, whose application in traditional medicine allows an insight into potential biological activities. Chemical composition of Zingiberaceae is: terpenoids, diarylheptanoids, arylalkaloides, phenylpropanoids, phenylbutanoids, flavonoids and related compounds[68].

4.6. Popular uses and economic importance

The Zingiberaceae contains many important species as hot spices, including *Zingiber* (*Z. officinale*, ginger)[69], turmeric (as domestic *Curcuma*), and *Amomum/ Elettaria* (as *Elettaria cardamomum*, cardamom). The rhizomes of many *Curcuma* species are used as a source of starch. *Alpinia*, *Curcuma*, *Hedychium* (butterfly flower), *Globba*, *Nicolaia*, *Zingiber* and *Renealmia* are ornamental species[43]. Other species have antiparasitic activities[70]. Many plants belonging to this family contain aromatic oils. In addition, species, such as ginger root (*Z. officinale*), which is used as a flavoring for wines, beers, soft drinks, and cakes, are of economic importance. Others are used in the dairy industry[71], also in the perfume industry, as medicinal or ornamental. Other uses are related to insecticides, molluscicide, nematicide and larvicide activities, which have also been reported as important properties of a series of compounds isolated from plants of this family[68]. Likewise, plants from the Zingiberaceae have been traditionally used against snakebites, a serious public health in tropical and subtropical areas[72]. It has been estimated that 5.5 million snakebite cases take place worldwide per year, some of which end in amputation of the affected limb (~8%) or loss of lives (~0.3% to ~2.3%)[3]. These events exceed the number of deaths from other tropical diseases such as hemorrhagic fever, dengue, cholera, leishmaniasis, and the Chagas disease[5]. Over 4 000 accidents per year take place in Colombia with a mortality that can reach 5% and with serious long-term effects in 6% of the survivors[73].

Table 3 lists plants from the Zingiberaceae used against snakebites in Eastern Antioquia[74]. One of the genera most relevant from the economic point of view is the genus *Alpinia*. The rhizomes of *Alpinia galanga* are commonly used for flavouring foods in Asia. Hot water extract from the rhizomes of *Alpinia galanga* is drunk for bronchitis and for diabetes in India[75,76]. The rhizomes boiled with *Curcuma*

Table 3

Plant species used to treat snakebites in Eastern Antioquia[74].

Species	Common name in the study area	Origin	No. informants	Part used	Administration form	Preparation form
Alpinia purpurata (Vieill.) K. Schum	Matandrea	Native	1	Leaves	Poultice	Maceration
R. alpinia (Rottb.) Maas	Matandrea blanca	Native	1	Leaves	Poultice	Maceration
				Stem	Chupadera	Direct heating
Renealmia aromatica (Aubl.) Griseb.	Matandrea blanca	Native	1	Leaves	Beverage	Maceration
				Stem	Chupadera	Direct heating
Renealmia cernua (Sw. ex Roem. & Schult.) J. F. Macbr.	Matandrea de moño rojo	Native	1	Leaves	Beverage	Maceration
Renealmia nicolaioides Loes.	Matandrea roja	Native	1	Leaves	Poultice	Maceration
				Stem	Chupadera	Direct heating

tubers in dilute vinegar and the vinegar extract is drunk for postpartum purification in Indonesia[77]. In Saudi Arabia a hot water extract of the rhizomes is used for dyspepsia, gasteralgia, chronic enteritis and anti-nausea and is also used for kidney stones[78,79]. The rhizome macerated in vinegar (acetic acid 2%) is used externally as an anti-inflammatory agent by applying to inflamed areas[80].

Additional biological activities have been reported, for example, an ethanolic extract of the rhizomes had anti-ascariasis, antibacterial, hypotensive and hypothermic and anti-fungal activity[81-84]. A methanolic extract of the rhizomes had anti-tumor activity[85]. Anti-ulcer activity and gastric secretory inhibition were found in the ethanolic extract of the rhizomes[86].

4.7. Pharmacological activities

The compounds isolated from a number of plants of this family possess a broad spectrum of biological and pharmacological activities. Therefore, various studies have demonstrated cytotoxic, antifungal, antibacterial, antimalarial, antihelminthic, anti-hepatotoxic, antioxidant, anti-ulcerative, anti-inflammatory and hypothermia, hypolipimedic, hypotensive, antitumor, spasmolytic and antinociceptive activities[68,87-98].

The Ophidism/ Scorpionism Program of the University of Antioquia held an evaluation about snakebite inhibitory effect of *B. asper* (mapaná) for the extracts obtained from leaves of *R. alpinia* Rottb. Maas (Zingiberaceae)[14,16].

5. Future perspectives and conclusion

R. alpinia has been used for indigenous in traditional medicine in South America. *In vitro* and *in vivo* pharmacological studies have increasingly confirmed its traditional use, especially on snakebite and pain. It is necessary to deepen studies of *R. alpinia* as a source of compounds that are active against the effects of snakebite. Furthermore, to correlate its pharmacological activity with its chemical components, and incidentally, to join forces in the search for new natural substances of pharmacological interest allow to improve life quality of patients, who can suffer an ophidian accident or a type of pain (acute or chronic), eventually finding that validated traditional knowledge become real and helpful possibilities.

The plants from the Zingiberaceae have been traditionally used in the treatment of various diseases, including poisoning caused by snakes. These plants are an excellent source of pharmacologically active metabolites, capable of neutralizing or partially/totally antagonize the effects caused by various factors. During a snakebite accident, these plants can neutralize the effects caused by the venom of snakes, constituting this family of plants in a set of promising alternative therapies to improve the prognosis and progression of various diseases. However it is important to direct the studies toward the chemical composition of plants and correlate this composition with potential pharmacological activity. In a word, phytochemical and pharmacological studies of *R. alpinia* have received much interest, extracts are been isolated and proved to have the anti-inflammatory, analgesic and anti-snakebite effects.

The studies available on toxicity and safety of *R. alpinia* are inadequate for providing information on ethnomedical utilization. Thus, the present review summarizes comprehensive information on *R. alpinia* and possible scope for future research to fill the existing lacunae on its different aspects of the study.

Finally, this review provides important information for the traditional use of plants in the Zingiberaceae family, the genus *Renealmia*, and especially *R. alpinia*. Furthermore, it stimulates the development of new work aimed to the study and production of metabolites with pharmaceutical interest using different technical support for the development of phytotherapeutic products, which can be inexpensive and accessible to the population. There are many areas to work in this plant for its full recognition; the present review summarizes complete information about *R. alpinia* and possible scope of future research to fill gaps in the study of various aspects of this plant species.

Conflict of interest statement

We declare that we have no conflict of interest.

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References

[1] Otero R, Fonnegra R, Jiménez SL, Núñez V, Evans N, Alzate SP, et al. Snakebites and ethnobotany in the northwest region of Colombia: Part I: traditional use of plants. *J Ethnopharmacol* 2000; **71**: 493-504.

[2] Gutiérrez JM, Williams D, Fan HW, Warrell DA. Snakebite envenoming from a global perspective: towards an integrated approach. *Toxicon* 2010; **56**: 1223-1235.

[3] Kasturiratne A, Wickremasinghe AR, de Silva N, Gunawardena NK, Pathmeswaran A, Premaratna R, et al. The global burden of snakebite: a literature analysis and modelling based on regional estimates of envenoming and deaths. *PLoS Med* 2008; **5**: e218.

[4] World Health Organization. Neglected tropical diseases. The 17 neglected tropical diseases. Geneva: World Health Organization; 2012. [Online] Available from: http://www.who.int/neglected_diseases/diseases/en/ [Accessed on 25th August, 2012]

[5] Williams D, Gutiérrez JM, Harrison R, Warrell DA, White J, Winkel KD, et al. The global snake bite initiative: an antidote for snake bite. *Lancet* 2010; **375**: 89-91.

[6] World Health Organization. Rabies and envenomings. A neglected public health issue. Geneva: World Health Organization; 2007. [Online] Available from: http://www.who.int/bloodproducts/animal_sera/Rabies.pdf [Accessed on 26th July, 2012]

[7] National Institute of Health. Annual ophidic accident 2012. Santafé de Bogotá: National Institute of Health; 2012. [Online] Available from: http://www.ins.gov.co/boletin-epidemiologico/Boletn%20Epidemiolgico/2012%20Boletin%20epidemiologico_Semana%2048.pdf.pdf [Accessed on 26th July, 2012]

[8] Orozco R. Antioquia Department, ophidic accident. Factors Risk Management Regional Health, Antioquia. 2012. [Online] Available from: http://www.dssa.gov.co/minisitio-dssa/index.php/diagnostico-de-la-situacion-salud/salud-ambiental?showall=&start=1[Accessed on 15th July, 2013] Spanish.

[9] Orozco R. Antioquia Department, ophidic accident. Factors Risk Management Regional Health, Antioquia. 2007-2012. 2012. [Online]Available from: http://www.dssa.gov.co/index.php/estadisticas/eventos-en-salud-publica [Accessed on 21st July, 2013] Spanish.

[10] Bon C. The serum: therapie was discovered 100 years ago. *Toxicon* 1996; **34**: 142-143.

[11] Lomonte B, Lundgren J, Johansson B, Bagge U. The dynamics of local tissue damage induced by *Bothrops asper* snake venom and myotoxin II on the mouse cremaster muscle: an intravital and electron microscopic study. *Toxicon* 1994; **32**: 41-55.

[12] Otero R, Núñez V, Jiménez SL, Fonnegra R, Osorio RG, García ME, et al. Snakebites and ethnobotany in the northwest region of Colombia: Part II: neutralization of lethal and enzymatic effects of *Bothrops* atrox venom. *J Ethnopharmacol* 2000; **71**: 505-511.

[13] Núñez V, Otero R, Barona J, Saldarriaga M, Osorio RG, Fonnegra R, et al. Neutralization of the edema-forming, defibrinating and coagulant effects of *Bothrops asper* venom by extracts of plants used by healers in Colombia. *Braz J Med Biol Res* 2004; **37**: 969-977.

[14] Patiño AC, Benjumea DM, Pereañez JA. Inhibition of venom serine proteinase and metalloproteinase activities by *Renealmia alpinia* (Zingiberaceae) extracts: comparison of wild and *in vitro* propagated plants. *J Ethnopharmacol* 2013; **149**: 590-596.

[15] Alarcón JC, Martínez DM, Quintana JC, Jiménez S, Díaz A, Jiménez I. [*In vitro* propagation of *Renealmia alpinia* (Rottb) plant against snakebite]. *Vitae* 2008; **15**: 61-69. Spanish.

[16] Patiño AC, López J, Aristizabal M, Quintana JC, Benjumea D. [Evaluation of the inhibitory effect of extracts from leaves of *Renealmia alpinia* Rottb. Maas (Zingiberaceae) on the venom of *Bothrops asper* (mapana)]. *Biomédica* 2012; **32**: 365-374. Spanish.

[17] Tropicos. Catalogue of the vascular plants of the Department of Antioquia (Colombia). Saint Louis: Missouri Botanical Garden; 2012. [Online] Available from: http://www.tropicos.org/Name/34500184?projectid=11&langid=12 [Accessed on 26th July, 2012]

[18] Corporation for the Sustainable Development of Southern Amazonia and Corpoamazonia. [Ecology, utilization and sustainable management of nine species of plants the department of Amazonas, generating timber and non-timber]. Bogotá: Corporation for the Sustainable Development of Southern Amazonia and Corpoamazonia; 2007. [Online] Available from: http://corpomail.corpoica.org.co/BACFILES/BACDIGITAL/55169/9especiesfinal.pdf [Accessed on 2nd July, 2014] Spanish.

[19] Macía MJ. *Renealmia alpinia* (Rottb) Maas (Zingiberaceae). Edible plant of the Sierra Norte of Puebla Mexico. *Anales Jardín Botánico De Madrid* 2003; **60**(1): 183-187.

[20] Acero LE. [*Top useful plants of the Colombian Amazon*]. Bogotá: Editora Guadalupe; 1979, p. 263. Spanish.

[21] Milliken W, Albert B. The use of medicinal plants by the Yanomami Indians of Brazil. *Econ Bot* 1996; **50**: 10-25.

[22] Villalobos CG, Contreras. [*Edible plants in two communities in the Sierra Norte of Puebla*]. Mexico: National Autonomous University of Mexico; 1994, p. 315.

[23] Martínez MA, Evangelista V, Basurto F, Mendoza M, Cruz-Rivas A. Useful plants of the Sierra Norte de Puebla, Mexico. *Rev Mex Biodiv* 2007; **78**: doi: 10.7550/rmb.5311.

[24] Lans C, Brown G. Observations on ethnoveterinary medicines in Trinidad and Tobago. *Prev Vet Med* 1998; **35**: 125-142.

[25] Standley PC, Steyermark JA. Zingiberaceae. In: *Flora of Guatemala. Fieldiana: Botany Vol 24, part III*. Chicago: Chicago Natural History Museum; 1952, p. 191.

[26] Gómez-Beloz A. Plant use knowledge of the Winikina Warao: the case for questionnaires in ethnobotany. *Econ Bot* 2002; **56**: 231-241.

[27] Lentz DL. Medicinal and other economic plants of the paya of Honduras. *Econ Bot* 1993; **47**: 358-370.

[28] Lentz DL, Clark AM, Hufford CD, Meurer-Grimes B, Passreiter CM, Cordero J, et al. Antimicrobial properties of Honduran medicinal plants. *J Ethnopharmacol* 1998; **63**: 253-263.

[29] Zhou BN, Baj NJ, Glass TE, Malone S, Werkhoven MCM, Van Troon F, et al. Bioactive labdanediterpenoids from *Renealmia*

alpinia collected in the Suriname rainforest. *J Nat Prod* 1997; **60**: 1287–1293.
[30] Ruysschaert S, Van Andel T, Van de Putte K, Van Damme P. Bathe the baby to make it strong and healthy: plant use and child care among Saramaccan Maroons in Suriname. *J Ethnopharmacol* 2009; **121**: 148–170.
[31] Ficker CE, Smith ML, Susiarti S, Leaman DJ, Irawati C, Arnason JT. Inhibition of human pathogenic fungi by members of Zingiberaceae used by the Kenyah (Indonesian Borneo). *J Ethnopharmacol* 2003; **85**: 289–293.
[32] Coe FG. Rama midwifery in eastern Nicaragua. *J Ethnopharmacol* 2008; **117**: 136–157.
[33] Camacho RL, López JAN, González MIM, Vecht KA, Castañeda MR, Barboza AP. [*Manual identification of non–timber species district of Tarapaca*]. Bogotá: Amazon Institute of Scientific SINCHI–German Technical Cooperation GTZ; 2006. Spanish.
[34] Lans C, Harper T, Georges K, Bridgewater E. Medicinal and ethnoveterinary remedies of hunters in Trinidad. *BMC Complement Altern Med* 2001; **1**: 10.
[35] Otero R, Nuñez V, Barona J, Fonnegra R, Jimenez SL, Osorio RG, et al. Snakebites and ethnobotany in the northwest region of Colombia. Part III: neutralization of the haemorrhagic effect of *Bothrops atrox* venom. *J Ethnopharmacol* 2000; **73**: 233–241.
[36] Valadeau C, Pabon A, Deharo E, Albán–Castillo J, Estevez Y, Lores FA, et al. Medicinal plants from the Yanesha (Peru): evaluation of the leishmanicidal and antimalarial activity of selected extracts. *J Ethnopharmacol* 2009; **123**: 413–422.
[37] de Mesquita ML, de Paula JE, Pessoa C, de Moraes MO, Costa–Lotufo LV, Grougnet R, et al. Cytotoxic activity of Brazilian Cerrado plants used in traditional medicine against cancer cell lines. *J Ethnopharmacol* 2009; **123**: 439–445.
[38] Fernández M, Ortíz WF, Pereáñez JA, Martínez D. [Antiophidian properties evaluation of ethanol extract and fractions obtained from *Renealmia alpinia* (Rottb.) Mass (Zingiberaceae) cultivated *in vitro*]. *Vitae* 2010; **17**: 75–82. Spanish.
[39] Arango G. Introduction to secondary metabolism, compounds derived from shikimic acid. Medellin: University of Antioquia; 2005. [Online] Available from: http://zh.scribd.com/doc/101839352/Introduccion–al–Metabolismo–Secundario [Accessed on 15th August, 2012] Spanish.
[40] Lognay G, Marlier M, Severin M, Haugruge E, Gibon V, Trevejo E. On the characterization of some terpenes from *Renealmia alpinia* Rottb. (Mass) oleoresin. *Flavour Fragr J* 1991; **6**: 87–91.
[41] Yang SW, Zhou BN, Malone S, Werkhoven MC, van Troon F, Wisse JH, et al. A new labdane diterpenoid from *Renealmia alpinia* collected in the Suriname rainforest. *J Nat Prod* 1999; **62**: 1173–1174.
[42] Särkinen TE, Newman MF, Maas PJ, Maas H, Poulsen AD, Harris DJ, et al. Recent oceanic long–distance dispersal and divergence in the amphi–Atlantic rain forest genus *Renealmia* L.f. (Zingiberaceae). *Mol Phylogenet Evol* 2007; **44**: 968–980.
[43] Maas PJM, Kamer HM. *Zingiberaceae, Flora de Nicaragua. Monographs in systematic botany from the Missouri Botanical Garden*. St. Louis: Missouri Botanical Garden; 2001, p. 2549–2554.
[44] Organization for Tropical Studies. [Flora digital jungle]. Costa Rica: Organization for Tropical Studies; 2006. [Online] Available from: http://sura.ots.ac.cr/local/florula2/families/ZINGIBERACEAE.pdf [Accessed on 15th August, 2012] Spanish.
[45] Kaplan MAC, Pugialli HRL, Lopes D, Gottlieb HE. The stereochemistry of ledol from *Renealmia chrysotrycha*: an NMR study. *Phytochemistry* 2000; **55**: 749–753.
[46] Tchuendem MHK, Mbah JA, Tsopmo A, Ayafor JF, Sterner O, Okunjic CC, et al. Anti–plasmodial sesquiterpenoids from the African *Renealmia cincinnata*. *Phytochemistry* 1999; **52**: 1095–1099.
[47] Williams CA, Harborne JB. The leaf flavonoids of the Zingiberales. *Biochem Syst Ecol* 1977; **5**: 221–229.
[48] Sekiguchi M, Shigemori H, Ohsaki A, Kobayashi J. Renealtins A and B, new diarylheptanoids with a tetrahydrofuran ring from the seeds of *Renealmia exaltata*. *J Nat Prod* 2002; **65**: 375–376.
[49] Luz AI, Zoghbi MG, Ramos LS, Maia JG, Silva ML. Essential oils of some Amazonian Zingiberaceae, genera *Alpinia* and *Renealmia*. *J Nat Prod* 1984; **47**: 907–908.
[50] Ramiandrasoa F, Chuilon S, Moretti C, Kunesch G. Labda–8(17), 12–diene–15, 16–dial, constituent of *Renealmia guianensis* (Zingiberaceae). *Plantes Medicinals et Phytotherapie* 1986; **20**: 227–230.
[51] Gu JQ, Park EJ, Vigo JS, Graham JG, Fong HH, Pezzuto JM, et al. Activity–guided isolation of constituents of *Renealmia nicolaioides* with the potential to induce the phase II enzyme quinone reductase. *J Nat Prod* 2002; **65**: 1616–1620.
[52] Selvanayahgam ZE, Gnanevendhan SG, Balakrishna K, Rao RB. Antisnake venom botanicals from ethnomedicine. *J Herbs Spices Med Plants* 1994; **2**: 45–100.
[53] Davis EW, Yost JA. The ethnomedicine of the Waorani of Amazonian Ecuador. *J Ethnopharmacol* 1983; **9**: 273–297.
[54] Maas PJM. *Renealmia (Zingiberaceae–Zingiberoideae)*. New York: New York Botanical Garden; 1977.
[55] Kress WJ, Prince LM, Williams KJ. The phylogeny and a new classification of the gingers (Zingiberaceae): evidence from molecular data. *Am J Bot* 2002; **89**: 1682–1696.
[56] Kala CP. Ethnomedicinal botany of the Apatani in the Eastern Himalayan region of India. *J Ethnobiol Ethnomed* 2005; **1**: 1–11.
[57] Pradhan BK, Badola HK. Ethnomedicinal plant use by Lepcha tribe of Dzongu valley, bordering Khangchendzonga Biosphere Reserve, in North Sikkim, India. *J Ethnobiol Ethnomed* 2008; **4**: 22.
[58] Larsen K. Further studies in the genus *Boesenbergia* (Zingiberaceae). *Nord J Bot* 1997; **17**: 361–366.
[59] Larsen K, Lock JM, Maas H, Maas PJM. *The families and genera of vascular plants.* Berlin: Springer Heidelberg; 1998.
[60] Larsen K, Jenjittikul T. *Laosanthus*, a new genus of Zingiberaceae from Laos. *Nord J Bot* 2001; **21**: 135–138.
[61] Theilade I, Mood J. Five new species of *Zingiber* (Zingiberaceae) from Borneo. *Nord J Bot* 1997; **17**: 337–347.
[62] Sakai S, Nagamasu H. Systematic studies of Bornean Zingiberaceae I. *Amomum* in Lambir Hills, Sarawak. *Edinburgh J Bot* 1998; **55**: 45–64.
[63] Tong SQ. *Paramomum*, a new genus of Zingiberaceae from Yunnan. *Acta Bot Yunnan* 1985; **7**: 309–312.
[64] Vovides AP. [Flora of Veracruz, Zingiberaceae]. Xaiapa: Institute of Ecology; 1994, p. 19. Spanish.

[65] Dahlgren RMT, Clifford HT, Yeo PF. *The families of the Monocotyledons: structure, evolution, and taxonomy*. Berlin: Springer-Verlag GmbH; 1985, p. 520.
[66] Angiosperm Phylogeny Website. Distribution of the Zingiberaceae family in the world. St Louis: Angiosperm Phylogeny Website; 2012. [Online] Available from: http://www.mobot.org/MOBOT/Research/APweb/welcome.html [Accessed on 12th May, 2012]
[67] Judd WS, Campbell CS, Kellogg EA, Stevens PF, Donoghue MJ. *Plant systematics: a phylogenetic approach*. 3rd ed. Sunderland: Sinauer Associates; 2007.
[68] Orasa P, Uma P, Pittaya T. Phytochemistry of the Zingiberaceae. *Stud Nat Prod Chem* 2000; **23**: 797-865.
[69] Pieroni A, Torry B. Does the taste matter? Taste and medicinal perceptions associated with five selected herbal drugs among three ethnic groups in West Yorkshire, Northern England. *J Ethnobiol Ethnomed* 2007; **3**: 21.
[70] Haddad M, Sauvain M, Deharo E. *Curcuma* as a parasiticidal agent: a review. *Planta Med* 2011; **77**: 672-678.
[71] Malik MH, Dong M, Muhammad FI, Chen X. Ginger rhizome as a potential source of milk coagulating cysteine protease. *Phytochemistry* 2011; **72**: 458-464.
[72] Mebs D. *Venomous and poisonous animals: a handbook for biologists, toxicologists and toxinologists, physicians and pharmacists*. Stuttgart: Medpharm Scientific Publishers; 2002.
[73] Otero R. *Snakebite poisoning. Fundamentals of pediatrics, Vol V: neurology, allergy, immunology, rheumatology, orthopedics, ENT and emergency*. 3rd ed. Medellín: Corporation for Biological Research; 2007.
[74] Vásquez J, Jiménez SL, Gómez IC, Rey JP, Henao AM, Marín DM, et al. Snakebites and ethnobotany in the Eastern region of Antioquia, Colombia, the traditional use of plants. *J Ethnopharmacol* 2013; **146**: 449-455.
[75] Chopra IC, Khajuria BN, Chopra CL. Antibacterial properties of volatile principles from *Alpinia galanga* and *Acorus calamus*. *Antibiot Chemother (Northfield Ill)* 1957; **7**: 378-383.
[76] Jain SR, Sharma SN. Hypoglycaemic drugs of Indian indigenous origin. *Planta Med* 1967; **15**: 439-442.
[77] Hirschhorn HH. Botanical remedies of the former Dutch East Indies (Indonesia). Part I: Eumycetes, Pteridophyta, Gymnospermae, Angiospermae (Monocotyledones only). *J Ethnopharmacol* 1983; **7**: 123-156.
[78] Rafatullah S, Tariq M, Al-Yahya MA, Mossa JS, Ageel AM. Evaluation of turmeric (*Curcuma longa*) for gastric and duodenal antiulcer activity in rats. *J Ethnopharmacol* 1990; **29**: 25-34.
[79] Ahsan SK, Shah AH, Tanira MO, Ahmad MS, Tariq M, Ageel AM. Studies of some herbal drugs used against kidney stones in Saudi folk medicine. *Fitoterapia* 1990; **6**: 435-438.
[80] Panthong A, Kanjanapothi D, Taylor WC. Ethnobotanical review of medicinal plants from Thai traditional books, Part I: Plants with anti-inflammatory, anti-asthmatic and antihypertensive properties. *J Ethnopharmacol* 1986; **18**: 213-228.
[81] Raj RK. Screening of indigenous plants for anthelmintic action against human *Ascaris lumbricoides*: Part II. *Indian J Physiol Pharmacol* 1975; **19**: 47-50.
[82] Bhakuni DS, Dhar ML, Dhar MM, Dhawan BN, Mehrotra BN. Screening of Indian plants for biological activity. II. *Indian J Exp Biol* 1969; **7**: 250-262.
[83] Tseng CF, Iwakami S, Mikajiri A, Shibuya M, Hanaoka F, Ebizuka Y, et al. Inhibition of *in vitro* prostaglandin and leukotriene biosynthesis by cinnamoyl-beta-phenethylamine and N-acyldopamine derivatives. *Chem Pharm Bull (Tokyo)* 1992; **40**: 396-400.
[84] Ross SA, Megalla SE, Dishay DW, Awad AH. Studies for determining antibiotic substances in some Egyptian plants. Part I. Screening for antimicrobial activity. *Fitoterapia* 1980; **51**: 303-308.
[85] Janssen AM, Scheffer JJ. Acetoxychavicol acetate, an antifungal component of *Alpinia galanga*1. *Planta Med* 1985; **51**: 507-511.
[86] Itokawa H, Morita H, Sumitomo T, Totsuka N, Takeya K. Antitumour principles from *Alpinia galanga*. *Planta Med* 1987; **53**: 32-33.
[87] Sulaiman MR, Perimal EK, Akhtar MN, Mohamad AS, Khalid MH, Tasrip NA, et al. Anti-inflammatory effect of zerumbone on acute and chronic inflammation models in mice. *Fitoterapia* 2010; **81**: 855-858.
[88] Oliveira F, Saito ML, Chunzum M. Caracterização morfológica da cana-do-brejo *Costus spiralis* (Jacquim) Roscoe- Zingiberaceae - Costoideae. *Rev Bras Farmacogn* 1986; **1**: 132-135. Spanish.
[89] Arawwawala LD, Arambewela LS, Ratnasooriya WD. *Alpinia calcarata* Roscoe: a potent antiinflammatory agent. *J Ethnopharmacol* 2012; **139**: 889-892.
[90] Zhang BB, Dai Y, Liao ZX, Ding LS. Three new antibacterial active diarylheptanoids from *Alpinia officinarum*. *Fitoterapia* 2010; **81**: 948-952.
[91] Chien TY, Chen LG, Lee CJ, Lee FY, Wang CC. Anti-inflammatory constituents of *Zingiber zerumbet*. *Food Chem* 2008; **110**: 584-589.
[92] Kader G, Nikkon F, Rashid MA, Yeasmin T. Antimicrobial activities of the rhizome extract of *Zingiber zerumbet* Linn. *Asian Pac J Trop Biomed* 2011; **1**: 409-412.
[93] de Araújo PF, Coelho-de-Souza AN, Morais SM, Ferreira SC, Leal-Cardoso JH. Antinociceptive effects of the essential oil of *Alpinia zerumbet* on mice. *Phytomedicine* 2005; **12**: 482-486.
[94] Darvishzadeh-Mahani F, Esmaeili-Mahani S, Komeili G, Sheibani V, Zare L. Ginger (*Zingiber officinale* Roscoe) prevents the development of morphine analgesic tolerance and physical dependence in rats. *J Ethnopharmacol* 2012; **141**: 901-907.
[95] Santos GKN, Dutra KA, Barros RA, da Câmara CAG, Lira DD, Gusmão NB, et al. Essential oils from *Alpinia purpurata* (Zingiberaceae): chemical composition, oviposition deterrence, larvicidal and antibacterial activity. *Ind Crops Prod* 2012; **40**: 254-260.
[96] Pongprayoon U, Tuchinda P, Claeson P, Sematong T, Reutrakul V, Soontornsaratune P. Topical antiinflammatory activity of the major lipophilic constituents of the rhizome of *Zingiber cassumunar*. Part II: hexane extractives. *Phytomedicine* 1997; **3**: 323-326.
[97] Victório CP. Therapeutic value of the genus *Alpinia*, Zingiberaceae. *Rev Bras Farmacogn* 2011; **21**: 194-201.
[98] Victório CP, Alviano DS, Alviano CS, Lage CLS. Chemical composition of the fractions of leaf oil of *Alpinia zerumbet* (Pers.) B.L. Burtt & R.M. Sm. and antimicrobial activity. *Rev Bras Farmacogn* 2009; **19**: 697-701.