Piper L. genus potential as natural biocide

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Summary

Plants synthesize distinct phytochemical compounds able to substitute synthetic biocides of difficult degradation; from this point of view, the extracts, essential oils and botanical origin compounds of some species, among them *Piper* genus, have been put forwarded as natural biocides, thanks to secondary metabolites presence which show different biological activity. It is true that there are about 1500 taxa described for *Piper* genus. However, less than one hundred have been studied concerning to their bioactivity. In this sense, the present research has as an objective to carry out a bibliographical review about the *Piper's* genus biocide potential. In this review, 50 taxa were found where biocide activity has been evaluated about some noxious organisms as plants, animals as humans; some of them considered plagues like *Spodoptera frugiperda* and *S. exigua*, others catalogued as disease vectors as *Aedes Aegypti*, human

and animal parasites such as; *Entamoeba hystolitica*, *Schistosoma mansoni* and *Trypanosoma evans*, of economic importance like *Melodoigyne incognita* and *Fusarium oxysporum* and even pathogenic microorganisms of medical importance such as; *Streptococcus pyogenes*, *Staphylococcus aureus* and *Mycobacterium tuberculosis*.

Key words: botanical compounds, biological activity, noxious organisms.

Introduction

Nowadays, mankind is looking for new alternatives that can help to heal the damage human being has made happen to the environment, these alternatives should be directed towards an ecological development. Among the handed options is the use of natural biocides capable to terminate, neutralize or wield some kind of control over every harmful organisms by chemical, physical or biological means (López Aguayo *et al*., 2010) Currently, the most used biocides are from botanical origin, which are extracted from plants by physicochemical methods that do not modify their chemical composition, besides they are not persistent in the environment and they are of easy degradation by UV light, assimilation and/or transformation caused by other organisms, these compounds can be one or several, belonging to plants' secondary metabolism, which do not have direct function in the development, however, it is well known these compounds play an important role in the defense of the plant and they are mediators in ecological interactions with other organisms, particularly, the defense and the attack of phytophagous**,** herbivorous animals, etc. This unusual peculiarity has made them strong candidates in biological control as natural biocides (Fernández and Juncoza, 2002; Sengonca *et al*., 2006; Celis *et al*., 2008; Wiratno *et al*., 2009; Dirzo, 1985; Heldt and Piechulla, 2004; Ernst-Detlef *et al.*, 2005; (Sepúlveda-Jiménez *et al*., 2003).

Basically, biocides properties of all plants are attributed to secondary metabolites and they can be equal or more effective depending on their chemical structure versatility, which varies from species to species or they can share with a group of species genetically related (Taiz and Zaiger., 2010). It is important to mention there are two groups of secondary compounds in plants, one group presents nitrogen in its structures, and the other is nitrogen free (Spring y Kutchan, 2009; Wink, 2010).

Alkaloids are examples of secondary metabolites that contain nitrogen in its structure, whose biological activity lies in the ability to block intermediary neuroreceptors of neuronal signal transduction and ionic channels of vertebrates and insects; meanwhile, their inhibitory effects in growth pathogenic microorganisms is given by their capacity of insert in DNA, as well as to inhibit the synthesis of proteins and carbohydrates, besides of inducing apoptosis (Sepúlveda *et al*., 2003).

Among free nitrogen compounds are flavonoids, they show bactericide activity in pathogen organisms interfering with their growing, similarly, flavonoids have a fungicide effect when inhibit digestive enzymes of some fungus, on the other hand, they are antiviral agents when inhibit and/or interfere with the viruses replication. (Martínez-Flores *et al*. 2002; Taiz and Zeiger, 2010; Bylka *et al*., 2004; Ogbemudia and Thompson; 2014, Spring y Kutchan, 2009). Another sort of metabolites of this group are terpenes, it is believed that these compounds are associated with the defense of the plant acting as toxins or phytolexins that repel insects and mammals. One more function of terpenes is the inhibition of bacteria and fungus growing, it is also believed they act as phytoecdisones for some insects as well. (Bennett and Wallsgrove, 1996; Taiz and Zeiger, 2010; Spring y Kutchan, 2009, Granados-Sanchez *et al*., 2008, Ogbemudia and Thompson; 2014).

It is possible to say that present compounds in plants are the searched alternatives to substitute synthetic biocides. So, a preamble is opened up to new alternatives present in plants; concerning to lines before, the present research had as main objective to carry out a bibliographical review about biological properties of genus *Piper* plant species, particularly, those that show some biocide effect.

Genus *Piper* classification, taxonomy and ecology

Piperaceae (Giseke) family, is considered as one of the most archaic lines of plants with blossom within pantropical flora, taking into account it is one of the most diverse lineages on earth containing between eight to ten genuses; approximately 3000 described species, although it is estimated they can be more (Scott *et al*., 2008; Quijano-Abril *et al*., 2006; Yung-Chien *et al*., 1999). This family belongs to Magnoliophyta division, in dycotiledonean class (Magliopsida) considered as the main representative of *Piperal* order. Its distributions is cosmopolitan in tropical and subtropical zones of the world, the American continent possess the major described species number (Yung-Chien *et al*., 1999; Greig, 2004; Jaramillo *et al*., 2004; Bottia *et al*., 2007; Jaramillo *et al*., 2008; Scott *et al*., 2008; Antonio de Souza, *et al*., 2009, Wanke *et al*., 2006).

Within this family, *Piperomia* and *Piper* genuses point out as the most representatives, the last one owns the biggest described species number with 1500 taxa approximately, distributed in nine sub-genuses: *Enckea*, *Radula*, *MacroPiper*, *Piper*, *Ottonia*, *Macrostachys*, *Schilleria*, *Pothomorpha*, *Peltobryon* and a complex called *Piper sanctum / P. cinereum* (Jaramillo *et al*., 2008, Jaramillo *et al*., 2004, Jaramillo and Manos, 2001).

Piper genus presents the following features; they are robust trees or sub-bushes, sometimes they are ivies or lianas, rarely hemiepiphyte, knotty, thicken stem; alternate leaves, complete, lanceolar, but often tied basally, they have palmribs or paralelribs ribs, sometimes foliar morphology varies in the same plant or species. Monopodic stems' leaves tend to be asymmetric and equilateral basally, while simpodic stems' leaves tend to be asymmetric and inequilateral basally. Petioles are from short to long and sometimes they are convolvulus, having sometimes very developed margins, visible stipules; inflorescences in terminal and solitary spadix opposite to leaves: sessile or pedicelled flowers frequently forming straps around the spadix, floral bracts, anthers and present pistil in the same blossom; fruit lightly distorted by the compression of adjacent, basally nailed or partially immersed in rachis. The vegetative part possesses the peculiarity to present scents when it is broken and it is easily melted in the hand fingers, most of them present lenticels (Yung-Chien *et al*., 1999; Jaramillo y Manos, 2001; Greig, 2004; Flemimg, 2004; Bornstein and Coe, 2007; Jaramillo *et al*., 2008; Jian and Jin-Ping Lui, 2011; Abreu-Guirado *et al*., 2012; Torres-Pelayo *et al*., 2014).

Another important characteristic of this genus plants is the sort of pollination, since it is known bats play an important role in it and both have suffered a coevolution along with *Piper* species, likewise, bats are in charge of disperse them. These plants can be found distributed along the tropical zone, and its altitudinal distribution range is not over a mile above the sea. *Piper* genus has most of its diversity in wet forest, lower mountains and lower lands. From those 1,500 reported species, approximately 1,000 taxa are distributed in Tropical America, which is considered the main diversification area of this genus, followed by Asia with 300 described species as it is showed in picture 1. (Jaramillo and Manos, 2001; Greig, 2004; Bornstein and Coe, 2007; Jaramillo *et al*., 2008; Jian and Jin-Ping Lui, 2011; Abreu-Guirado *et al*., 2012; Torres-Pelayo *et al*., 2014).

***Piper*'s phytochemical compounds and its biocide effect**

Within the world ambit of photochemistry, genus *Piper* is well thought-out as one of the most studied plants regarding others. Within this group, around 667 different bio-actives have been characterized and they continue increasing along the years, among the most common compounds for genus *Piper* species, around 49 lignines, 79 neolignines, 97 terpenes, 39 propenylphenols, 15 steroids, 18 kawapirones, 17 chalcones/dihydrochalcones, 16 flavones, 6 flavonones and 4 piperolides have been isolated (Dyer Lee *et al.*, 2004; Parmar *et al*., 1997). In the year 2012, the presence of 277 alkaloids/amides synthesized by *Piper* species were reported, *Piperina* has been the most frequent, whose chemical structure is based on a double ring with a simple chain of Piperonyl CoA, linked to a Piperidina ring (picture 2). In the figure, the chemical structure of the most common secondary metabolites of *Piper* genus is shown. (Nascimento *et al*., 2012; Okwute and Egharevba, 2013).

Sterols are also present in *Piper* genus compounds; such as, sisterol and stigmasterol, majority flavonoid like 7,4-dimetoxy-5-hydroxyflavone, quercetin, kaempherol, tectocrisine and pinostrobine; terpenes like α- terpinine, γ-terpenine, terpinolene, α-thujene, transphytol, limonine and linalool. Propenylphenol as myristicine, pseudodillapiol, saphrol, eugenol, eugenol methyl ether and elemicine; among alkaloids/amides present we can find cepharadione A and B, guineecine, (2E, 4E)-N-isobutyldecadienamide, pipericide, piperine, piperine S, piplartine, piperlonguminine, among others (Parmar *et al*., 1997, Bottia, 2007).

Biocide activity of *Piper* genus (insecticide, fungicide, nematicide and bactericide) has been associated to the toxicity of its phytochemical compounds mainly piperamides, which are quinolizinical alkaloids with an amide group (Dyer Lee *et al*., 2004) this ensemble compounds can be found in all species of *Piper* genus, in Asia is known that Piperine is the main compound responsible for the biocide activity of *Piper nigrum* and *P. betel.* Other biological properties possessed by these compounds are; stimulant for the central nerve system, analgesic, antipyretic and anti-inflammatory, to the rest of the *piper* species, other amides have been reported containing the same properties (Parmar *et* al., 1997; Dyer Lee *et al*., 2004; Chansang, *et al*., 2005; Chahal *et al*., 2011, Nascimento *et al*., 2012).

The toxic action of these alkamides lies on the way of act, since they act like neurotoxins, avoiding the shift of voltage between the ionic channels as in Na+ as in Ca++ in insects, invertebrates and mammals (Scott *et al*., 2008; Okwute and Egharevba, 2013; Ntalli and Caboni, 2012). In the case of unicellular organisms its effect happens in a genetic level (Bezerra, 2009).

It should be added that some phenolic compounds present in some plants of this genus, also present biocide activity. For instance, the characterized compound like dillapiol has shown effects highly clasthogenic in genetic material of *Aedes aegipty* (Rafael *et al*., 2008). Equally, has been reported that some essential oils rich in fatty acids, terpenes, and phenolic compounds have repellent effect in some diptera (Misni *et al*., 2008)

Piper's **species biological activity**

The biological activity present in many species of genus *Piper* has been widely studied along the last years and recently new contributions about the bio potential of this genus have been incorporated, pointing out the bactericide, fungicide, insecticide, anti-parasitic, nematicide activity, among others: Below the species and their effects in organisms are broken down and described in which this activity has been proved. Some of the organisms are showed in table 1, where it is possible to see the organisms used to prove the biological effects of the extracts, as well as the essential oils and phytochemical compounds isolated from distinct *Piper* genus species.

Bactericide activity

Bacteria is defined as microscopic and unicellular microorganisms capable to cause damage; as human health as plants and animals. In this context, the bactericide effect of *Piper* genus plants has been evaluated in the long run, some of them have showed to have a biocide effect on relevant bacteria, such as: *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis*, *Staphylococcus epidermis* and *Enterobacter cloaceae* (Rodrigues-Silva *et al*., 2009) Similarly the same effect happens on bacteria *Streptococcus pyogenes, Proteus vulgaris, Salmonella tiphy* (Chakraborty and Shah, 2011) in *Klebsiella pneumoniae, Pseudomona aeruginosa*, (Zakaria *et al*., 2007; Benítez *et al*., 2009).

Its effect is also known in negative gram bacteria, such as: *Streptococcus salivarius, Streptococcus mutans, Streptococcus sanguinis, Streptococcus mitis, Bacillus cerus, Salmonella typhimurium, Staphylococcus lentus, Enterobacter cloaceae, Alicyclobacillus acidoterrestris, Enterococcus faecalis, Helicobacter pilory, Mycobacterium tuberculosis* (Silva *et al*., 2007, Karsha and Lakshme, 2010, Zaidi *et al*., 2009, Scodro *et al*., 2013, Akthar *et al*., 2014).

Other important effects of some *Piper* species have been proved in phytobacteria responsible for crop diseases like: *Xanthomonas albilineas, X. campestris, P. solanacerum, P. celebensis, P. syzygii, P. fluorescens* and *Acidovorax* *avenae* (Sánchez *et al*., 2014, Sánchez *et al*., 2013, Sánchez *et al*., 2011, Sánchez *et al*., 2009, Pérez *et al*., 2015).

Fungicide activity

This activity has proved its effect on some fungus, many of them contemplated as plagues like the case of *Fosarium oxysporum* a phytopathogen that affects tomato commercial plantations, as well as other plants of great importance (Singha *et al*., 2011). *Botryodiplodia theobromae* causes gummosis in citrus, *Colletotrichum acutatum* and *Colletotrichum gloeosporioides,* they affect mango, papaya, and citrus plantations producing anthracnose and premature falling of the fruit in citrus (Pineda *et al*., 2012; Barquero *et al*., 2013). The fungicide effect has also been proved in phytopathogen fungus *Curvularia lunata*, *Sarocladium oryzae* and *Bipolaris oryzae* which are associated to damages and tissue diseases in some cereals (Duarte *et al*., 2014), in *Hemileia vastatrix* known as the blight coffee plants, as well as in *Cercospora coffeicola*, *C. gloeosporioides* and *Rhizoctonia solani*, fungus that attack coffee plantations (Silva *et al*., 2014).

In the same tenor, anti-candida activity has been found (*Candida krusei*, *C. parapsilosis*, *C. albicans*, *C. tropicalis* and *C. glabrata*) on the side of species of this genus and over other fungus of medical importance like *Microsporum gypseum*, *M. canis*, *Trichophyton rubrum*, *Apergilus flavus*, *A. fumigatus*, and *Cryptococus neoformans* (Regasini *et al*., 2009; Palacios *et al*., 2009; Rodrigues-Silva *et al*., 2009; Intzar *et al*., 2010; Morandim-Giannetti *et al*., 2010).

Insecticide activity

The insecticide effects is the most studied pesticide area in recent years, concerning to this activity in the *Piper* genus species. It has been proved, in at least eleven organisms, the biocide action of these compounds. Some of the organisms where this bioactivity has been proved are *Drosophila melanogaster* and *Musca domestica* (Carmona-Hernández *et al*., 2014; Torres-Pelayo, 2014; Rafael *et al*., 2008, Misni *et al*., 2008; Choochote *et al*., 2006 Jensen *et al*., 2006; Jensen *et al*., 2005, Granados *et al*., 2002; Kong *et al*., 2009, Moreno *et al*., 2000, Sanabria *et al*., 2009).

In plague organisms, this activity has been evaluated in vegetable extracts like essential oils of different *Piper* genus species, where the result have been toxic effects on vectors, such as: *Anopheles pseudopunctipennis, Lutzomyia migonei, Rhipicephalus microplus, Aedes atropalpus* and *Aedes aegypti* (Scott *et al*., 2005, Bazán-Calderón *et al*., 2011, Leyva *et al*., 2009, Nieves *et al*., 2010, García-Paz, 2011, Ferraz *et al*., 2010). On the other hand, there are phytophagous organisms where the biocide effect was proved, among them are: *Malacosoma americanum,* which causes injuries in leaves of cherries and apples, *Neodiprion sertifer,* the pines defoliator (Celis *et al*., 2008, Scott *et al*., 2004) *Diatrea saccharalis*, the reed borer, which affects both sorghum and corn (Tavares *et al*., 2011, Soberón *et al*., 2006). *Hyphothenemus hampei* the coffee plants driller, it damages mainly fruits (Mosquera *et al*., 2009), *Sitophilus zeamais*, corn weevil that affects the grains during storage in warehouses (Asawalam, 2006). *Spodoptera frugiperda* corn and other grasses earworm (Tavares *et al*., 2011) *S. exigua*, lettuce and other vegetable earworm (Delgado-Barreto *et al*., 2012) *Rhizotrogus majalis,* Beetle of European origin known as *chaflan*, it damages grass roots (Scott *et al*., 2005). Likewise there has been reported insecticide activity in garden organisms (Scott *et al*., 2007; Scott *et al*., 2008).

Nematicide and anthelmintic activity

In the field of biocide action, there are a few records about nematicide and anthelmintic potential of *Piper* species. However, some reports talk about toxicity in *P. betel, P. nigrum, P. longum* and *P. aducum*; in *Pheretima posthuma* and *Haemonchus contortus,* parasite worms in human and animal bowels; their contribution to health damage can be serious whether they are not treated on time. Also, some nematicide effect has been found on behalf of *P. betel* and *P. nigrum* in *Meloidogyne incognita* this is a phytonematode of economic importance, since it is mainly a parasite in a wide variety of plants of nutritious interest, among them are; tomato, potato, coffee and others. This phytonematode causes nodules in plants' roots, and injuries in a tissue level, which provokes wounds and access to other noxious organisms that damage or even kill plants

(Devi *et al*., 2011; Lopes Oliveira *et al*., 2014; Dammini Premachandra *et al*., 2014; Wiratno *et al*., 2009; Evans *et al.*, 1984). In the same way, there are other *Piper* species reports having biocide effect over medical importance nematodes, such as: *Paramphistomum epiclitum* responsible for paramphistomiasis in cows and sheep, as well as *Schistosoma mansoni*, author of the human disease schistomatosis or bilharzia (Atjanasuppat *et al*., 2009).

Antiprotozoal activity

Protozoa are unicellular organisms of free life and forced parasite or semi parasite from different living beings, they trigger lethal diseases if they are not healed on time, and an example of them is paludism or malaria, caused by several species of *Plasmodium* genus, leishmaniasis induced by *Leishmania sp*. or giardiasis provoked by *Giardia lanblia*, sarcoidosis by *Sarcocystis hominis* and amebiasis by diverse species of *Entamoeba* (Pérez-Arellano *et al*., 2007). In this context, *Piper* species like *P. nigrum*, *P. amalago, P. ovatum* and *P. longum* have been studied to evaluate the activity over protozoa which cause diseases, they have been proved in *Entamoeba histolytica*, *Leishmania amazonensis*, *Trypanosoma evansi* and *Acanthamoeba polyphaga*, it is still looking for products capable of inhibit these microorganisms (Carrera *et al*., 2013; Sauter *et al*., 2012; Shaba *et al*., 2012; Rodríguez-Silva *et al*., 2009; Sawangjaroen *et al*., 2004; Ghoshal *et al*., 1996).

Conclusions

Species of *Piper* genus are wide distribution plants of arboreal, shrubby and quickly reproduction habits, they represent a natural resource with a great biotechnological potential in the quest of compounds with biocide activity, adequate to the new tendency of biodegradable nature products and ecologically acceptable. Phytochemical compounds proceeding from secondary metabolism of *Piper* species can be used as biological control over noxious organisms due to their toxicity of widespread spectrum. They have proved to be a good prospect product used as a natural biocide, as a result of their extracts and/or essential oils chemical composition, furthermore they have a botanical source and they are environment friendly. The present potential in *Piper* species, is an alternative that should be exploited within scientist scope to discover some more about the effects that 1500 reported species of this genus have and their more than 665 participant compounds in their bactericide, fungicide, insecticide, nematicide, antiprotozoal and anthelmintic activity. Finally, it is possible to say genus *Piper* contains the necessary potential to be used as natural biocide without damaging the environment. In addition, its phytochemical compounds are versatile from one species to another, giving unique biocides characteristics which ply not the same effect on each noxious or pathogenic organism.

References

Abreu-Guirado O. A., A. A. Rodriguez-Tamargo, M. Morgano-Montes y L. B. Cao Vocero. (2012). Farmacognosia, farmacobotánica, farmacogeografía y farmacoetimología del platanillo de Cuba (Piper aduncum subespecie ossanum). Revista Cubana de Plantas Medicinales 17(2): 181-193.

Ahmad, F., Sirat, H. M., Jamaludin, F., Mustapha, N. M. A., Ali, R. M., Arbain, D., & Aboul-Enein, H. Y. (2014). Antimicrobial and anti-inflammatory activities of *Piper porphyrophyllum* (Fam. Piperaceae). *Arabian Journal of Chemistry*, *7*(6), 1031-1033.

Akthar, M. S., Birhanu, G., & Demisse, S. (2014). Antimicrobial activity of Piper igrum L. and Cassia didymobotyra L. leaf extract on selected food borne pathogens. *Asian Pacific Journal of Tropical Disease*, *4*, S911-S919.

Antonio de Souza, L., I. Sebastiao Moscheta, K. S. Mathias Mourao, A. L. Meyer Albeiro, M. Carvalho Iwazaki, L. H. Georg Oliver and S. Maciel da Rosa.

(2009). Vegetative Propagation in Piperaceae Species. Braz. Arch. Biol. Technol. v.52 n. 6: pp. 1357-1361.

Asawalan, E. F. (2006). Insecticidal and repellent properties of *Piper guineense* seed oil extract for the control of maize weevil, *Sitophilus zeamais.* EJEAFChe, *5 (3):* 1389-1394.

Ashish Patil, M. and S. Annasaheb Niyave. (2014). Comparative Anthelmintic activity and phytochemical evaluation of *Tridax procumbens* Linnwhole plant extract and *Piper nigrum* Linn seed extract on indian adult earthworm. Int. J. Pharm. Sci. Rev. Res., 27(2): 54-57.

Atjanasuppat, K., Wongkham, W., Meepowpan, P., Kittakoop, P., Sobhon, P., Bartlett, A., & Whitfield, P. J. (2009). In vitro screening for anthelmintic and antitumour activity of ethnomedicinal plants from Thailand. *Journal of ethnopharmacology*, *123*(3), 475-482.

Ávalos, G. A. y E. Perez-Urria C. (2009). Metabolismo secundario de plantas. Reduca (Biologia). Serie Fisiología Vegetal 2 (3); 119-145.

Bazán-Calderón J, R. Ventura-Flores, M. J. Kato, C. Rojas-Idrogo, . E. Benítez N. P. E, M. E. and Stashenko E. 2009. Composición química y actividad antibacteriana del aceite esencial de hojas de *Piper lanceaefolium,* planta usada tradicionalmente en Colombia. Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas, 8(4): 301-304.

Bazán-Calderón, J., Ventura-Flores, R., Kato, M. J., Rojas-Idrogo, C., & Delgado-Paredes, G. E. (2011). Actividad insecticida de *Piper tuberculatum* Jacq. sobre *Aedes aegypti* L.(Diptera: Culicidae) y Anopheles pseudopunctipennis Tehobal (Diptera: Culicidae).

Benítez, N. P. E. Melendez y E. E. Stashenko. (2009). Composición química y actividad antibacteriana del aceite esencial de hojas de *Piper lanceaefolium,* planta usada tradicionalmente en Colombia. Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas 8 (4); 301 – 304.

BennettRN, W. (1994). Secondary metabolites in plant defence mechanism. New Phytol 127, 617-63310.

Bezerra, D. P., Vasconcellos, M. C., Machado, M. S., Villela, I. V., Rosa, R. M., Moura, D. J., ... & Costa-Lotufo, L. V. (2009). Piplartine induces genotoxicity in eukaryotic but not in prokaryotic model systems. Mutation Research/Genetic Toxicology and Environmental Mutagenesis, 677(1), 8-13.

Bornstein and F. G. Coe. (2007). The genus *Piper* (Piperaceae) in Honduras. Novon: A Journal for Botanical Nomenclature 17(1):11-19.

Bottia, S., E.J., O. L. Díaz F. D. L. Mendivelso, J. R. Martínez, E. E. Stashenko. (2007). Comparación de la composición química de los metabolitos volátiles de cuatro plantas de la familia piperaceae obtenidos por destilación-extracción simultánea. Scientia Et Technica 13(33): 193-195.

Brazao, M. A. B., Brazao, F. V., Maia, J. G. S., and Monteiro, M. C. (2014). Antibacterial activity of the Piper aduncum oil and dillapiole, its main constituent, against multidrug-resistant strains. *Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas*, *13*(6), 517-526.

Bylka, W., Matlawska, I., & Pilewski, N. A. (2004). Natural flavonoids as antimicrobial agents. Jana, 7(2), 24-31.

Carmona-Hernández, O., M. S. Fernández, B. Palmeros Sánchez y J. A. Lozada García. (2014). Actividad insecticida de etractos etanólicos foliares de nueve piperáceas (*Piper* spp.) en Drosophila melanogaster. Rev. Int. Contam. Ambient. vol 30 pp. 67-73

Carrara, V. D. S., Cunha-Júnior, E. F., Torres-Santos, E. C., Corrêa, A. G., Monteiro, J. L., Demarchi, I. G. y Cortez, D. A. G. (2013). Antileishmanial activity of amides from Piper amalago and synthetic analogs. *Revista Brasileira de Farmacognosia*, *23*(3), 447-454.

Celis A., C. Mendoza, M. Pachón, J. Cardona, W. Delgado y L. E. Cuca. (2008). Extractos vegetales utilizados como biocontroladores con énfasis en la familia Piperaceae. Una revisión. Agronomía Colombiana 26(1); 97-106

Chahal JR, Ohlyan A, Kandale A, Walia and Puri S. 2011. Introduction, phytochemistry, traditional uses and biological activity of genus *Piper*: a review. IJCPR, 2(2): 131-144.

Chakraborty D. and B. Shah. (2011). Antimicrobial,anti-oxidative and anti-hemolytic activity of *Piper betel* leaf extracts. J Pharm Pharm Sci, 3 (3): 192-199.

Chansang U, S. Z. N. S. Zahiri, J. Bansiddhi, T. Boonruad, P. Thongsrirak, J. Mingmuang, N. Benjapong and M. S. Mulla. (2005). Mosquito larvicidal activity of aqueous extracts of long pepper (*Piper retrofractum)* from Thailand. J Vector Ecol 30(2):195-200.

Choochote W., U. Chaithong, K. Kamsuk, E. Rattanachanpicha, A. Jitpakdi, P. Tippawangkosol, D. Chaiyasit, D. Champakaew, B. Turtun and B. Pitasawat. (2006). Adulticidal activity agaist *Stemomyia aeqyti* (Diptera: Culicidae) of three *Piper spp.* Rev.Inst. Med. Trop. S. Paulo. 48(1):33-37.

Dammini Premachandra, W.T.S, H. Mampitiyarachchi and L. Ebssa. (2014). Nemato-toxic potencia of Betel (*Piper betle* L.) (Piperaceae) leaf. Crop Protection 65 1-5.

Datta, A., Ghoshdastidar, S., and Singh, M. (2011). Antimicrobial property of piper betel leaf against clinical isolates of bacteria. *Int J Pharm Sci Res*, *2*(3), 104-109.

Delgado Barreto, E., García-Mateos, M., Ybarra-Moncada, M., Luna-Morales, C., & Martínez-Damián, M. (2012). Propiedades entomotóxicas de los extractos vegetales de *Azaradichta indica*, *Piper auritum* y *Petiveria alliacea* para el control de *Spodoptera exigua* Hübner. *Revista Chapingo. Serie horticultura*, *18*(1), 55-69.

Devi, M. S., y Kumar, B. S. (2011). Anthelmintic activity of thirikadugu chooranam and its ingredients. *Asian Journal of Pharmaceutical and Clinical Research*, *4*(3), 58-60.

Diego, L. (2012). Chemical composition and antifungal activity of Piper auritum Kunth and Piper holtonii C. DC.against phytopathogenic fungi. *Chilean Journal of Agricultural Research*, *72*, 4.

Dirzo, Rodolfo. (1985). Metabolitos secundarios en las plantas, ¿Atributos panglossianos o de valor adaptativo?. Ciencia 36: 137-145

Duarte, Y., Pino, O., & Martínez, B. (2014). Efecto de cuatro aceites esenciales sobre hongos asociados al manchado del arroz. *Revista de Protección Vegetal*, *29*(1), 62-65.

Dyer, Lee A., J. Richars and C. D. Dodson. (2004). Chapter 2: Insolation, synthesis and evolutionary ecology of Piper Amides. Piper: A model genus for studies of phytochemistry, ecologu and evolution. 117-139 p

Ernst-Detlef S., E. Beck and K. Müller-Hohenstein. (2005). Chapter 1.10; Biotic stress: herbivory, infection, allelopathy. Plant Ecology. Springer-Verlag Berlin Heiderlberg. Germany. 235-254 p.

Evans H. P., w. s. Bowers and E. J. Funk. Indentification of fungicidal and nematocidal components in the leaves of *Piper betle* (Piperaceae)

Fernández, C. y R. Juncosa. (2002). Biopesticidas: ¿la agricultura del futuro?. *Phytoma* 141:14-19.

Ferraz, A. B. F., J. M. Balbino, C. Alcara Z., V. L. Ribeiro, S. A. L. Bordignon and G. von Poser. (2010). Acaricidal. Acaricidal activity and chemical composition of the essential oil from three *Piper* species. Parasitol 107:243–248.

Fleming, T. H. 2004. Chapter 4. Dispersal ecology of neotropical *Piper* shrubs and trelets. *Piper* a model genus of studies of phytochemesty, ecology and evolution. Kluwer Academy; Plenum Publishers. New York.

García-Paz, J.L. (2011). Evaluación de las propiedades acaricidas de *Piper crassinervium* Kunth. *Piper aequale* Valh. (Piperaceae) sobre larvas de *Rhipicephalus (Boophilus) microplus* (Canestrini, 1887)(Acari:Ixodidae). Tesis para obtener el grado de Maestro en Ciencias. Facultad de ciencias Agropecurias. Universidad Nacional de Colombia 96 p.

Ghoshal, S., Prasad, B. K., & Lakshmi, V. (1996). Antiamoebic activity of Piper longum fruits against Entamoeba histolytica in vitro and in vivo. *Journal of ethnopharmacology*, *50*(3), 167-170.

Granados, H. N., J. Sáez , C. Robles, L. F. Vázquez, M. E. Moreno, J. M. Acevedo, C. A. Peláez y R. Callejas. (2002). Evaluacion de la actividad insecticidad de extractos de *Piper grande* Vahl (Piperaceae) en el modelo biológico: *Drosophila melanogaster*. Rev. Fac. Nal. Agr. Medillín. 55(2):1601-1613.

Granados-Sánchez, D., P. Ruíz-Puga y H. Barrera-Escorcia. (2008). Ecologia de la Herbivoria. Revista Chapingo Serie Ciencias Forestales y del Ambiente 14(1):51-63

Greig, N. (2004). Chapter 1. Introduction. *Piper*: A Model Genus for Studies of Phytochemistry, Ecology, and Evolution. Kluwer Academy; Plenum Publishers. New York.

Heldt, H. W., & Piechulla, B. (2004). Plant biochemistry. Academic Press.

Intzar Ali, F. G Khan, K. A. Suri, B. D. Gupta, N. K. Satti, P. Dutt, F. Afrin, G. N Qazi, I. A. Khan. (2010). In vitro antifungal activity of hydroxychavicol isolated from *Piper betle* L. Annals of Clinical Microbiology and Antimicrobials. 9 (7).

Jaramillo, M. A. and P. S. Manos. (2001). Phylogeny and patterns of floral diversity in the genus *Piper* (Piperaceae). American Joural of Botany. 88 (4): 706 -716.

Jaramillo, M. A., & Callejas, R. (2004). Current Perspectives on the Classification and Phylogenetics of the Genus Piper L. In *Piper*: a model genus for studies of phytochemistry, ecology, and evolution (pp. 179-198). Springer US.

Jaramillo, M. A., Manos, P. S., & Zimmer, E. A. (2004). Phylogenetic relationships of the perianthless Piperales: reconstructing the evolution of floral development. International Journal of Plant Sciences, 165(3), 403-416.

Jaramillo, M. A., R. Callejas, C. Davidson, J. F. Smith, A. C. Stevens and E. J. Tepe. (2008). A phylogeny of the Tropical Genus *Piper* Using ITS and the Chloroplast Intron psbj-petA. Systematic Botany 33(4): 647–660.

Jensen, H. R. I. M. Scott. S. R. Sims, V. L. Trudeau and J. T. Arnason. (2006). The effect of a synergistic concentration of a *Piper nigrum* extract used in conjunction whit pyrethrum upon gene expression in *Drosophila melanogaster*. Insect Molecular Biology 15(3)329-339.

Jensen, H. R., I. M. Scott, S. Sims, V. L. Trudeau and J. T. Arnason. (2005). Gene expression profiles of *Drosophila melanogaster* exposed to an insecticidal extract of *Piper nigrum*. Journal of Agriculture and Food Chemistry. J Agric Food Chem 54:1289–1295

Jiang Yang and Jin-Ping Lui. (2011). Analysis of genetic diversity of *Piper* spp. In Hainan Island (Chiana) using inter-simple sequence repeat ISSR marker. African Journal of Biotechnology Vol. 10(66), 14731-14737.

Karsha, P. V., & Lakshmi, O. B. (2010). Antibacterial activity of black pepper (Piper nigrum Linn.) with special reference to its mode of action on bacteria. *Indian J Nat Prod Resour*, *1*(2), 213-215.

Kong, C M., S. Sulaiman and H. Othaman. (2009). Efficacy of *Piper aduncum* extract against the adult Housefly (*Musca domestica*). J Trop Med Parasitol. 32(2): 52-57.

Lopes Oliveira, T. M. Viera, V. F. Nunes, M. Oliveria Ruas, E. R, Duarte, D. Lima Moreira, M. A. Coelho Kaplan y E. Ronie, Martins. (2014). Chemical composition and efficacy in the egg-hatching inhibition of essential oil Piper aduncum against Haemonchus contortus from sheep. Rev Bras Farmacogn vol. 24: pp. 288-282.

López Aguayo, M. C., Grande Burgos, M. J., Lucas López, R., & Gálvez, A. (2010). Resistencia a biocidas de diferentes cepas de *Escherichia coli*. Anales de la Real Academia de Ciencias Veterinarias de Andalucía Oriental, (23), 121-136.

Martínez-Flores, S., J. González-Gallego, J. M. Culebras y M. J. Tuñón. (2002). Los flavonoides: Propiedades y acciones antioxidantes. Nutr. Hosp. 8 (6): 271-278.

Mazid, M., T. A. Kha y F. Mohammand. (2011). Role of secondary metabolites in defense mechanism of plants. Biology and Medicine, Vol 3 (2): 232-249

Mesa, C. A., J. Montiel, C. Martinez, B. Zapata, N. Pino, J. G. Bueno y E. Stashenko. (2007). Actividad *in vitro* anti-*Candida* y anti-A*spergillus* de aceites esenciales de plantas de la familia piperaceae. Scientia et Technica Año XIII, No33: 247-249

Misni N., S. Salaiman and H. Othaman. (2008). The repellent activity of *Piper aduncum* Linn (Family: Piperaceae) essential oil against *Aedes aegypti* using Human volunteers. J Trop Med Parasitol. 31: 63-9.

Morandim-Gionneti, A. A., A. R. Pin, N. A. S. Pietro, H. C. Oliveira, M. J. S. Mendes-Giannini, A. C. Alecio, M. J. Kato, J. E. Olivera and M. Furlan. (2010). Composition and antifungal activity against *Candida albicans*, *Candida parapsilosis*, *Candida krusei* and *Cryptococcus neoformans* of essential oils from leaves of *Piper* and *Peperomia* species. Journal of Medicinal Plants Research 4(17): 1810-1814.

Moreno, M. E., S. González, L. Acevedo, G. Morales, M. Betancur, J. J. López y C. A. Peláez. (2000). *Drosophila melanogaster* (Diptera: Drosophilidae): modelo biológico para la estandarización de extractos naturales con actividad insecticida (El Neem- *Azadirachta indica*- un caso particular). Revista entomológica de Colombia 26 (1-2) 21-55.4

Mosquera, M. O., L. M. Henao y J. Niño. (2009). Evaluación de la actividad insecticida *in vitro* de extractos vegetales contra la broca del café. Recursos Naturales y Ambiente. 58: 45-50.

Nascimento, J. C., V. F. de Paula, J. M. David and J. David. (2012). Occurrence, biological activities and CNMR data of amides from *Piper* (Piperaceae). Quim. Nova, Vol. 35 (11); 2288-231.

Nieves, E., Méndez, J. F., Lias, J., Rondón, M., & Briceño, B. (2009). Actividad repelente de aceites esenciales contra las picaduras de *Lutzomyia migonei* (Diptera: Psychodidae). *International Journal of Tropical Biology and Conservation*, *58*(4).

Ntalli, N. G. and P. Caboni. 2012b. Botanical nematicides: a review. J. Agric. Food Chem. 60: 9929-9940.

Ogbemudia, F. O. and E. O. Thompson. (2014). Variation in plants secondary and potential ecological roles a review International Journal of Modern Biology and Medice 5(3): 111-130.

Okwute, S. K., & Egharevba, H. O. (2013). Piperine-Type Amides: Review of the Chemical and Biological Characteristics. International Journal of Chemistry, 5(3), p99.

Olivero-Verbel J, Güette-Fernández J and Stashenko E. (2009). Acute toxicity against Artemia franciscana of esencia oils isolated from plants of the genus Lippia and Piper collected in Colombia. Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas, 8(5): 419 – 427.

Palacios Z. G. F., G. E. Delgado, M. C. Moreno, M. J. Kato y C. Rojas. (2009). Actividad antifúngica *in vitro* de extractos crudos de *Piper tuberculatum*. *Rev. peru. biol.* 16(2): 209 – 214.

Parmar, V. S., S. C. Jain, K. S. Bisht, R. Jain, P. Taneja, A. Jha, Om D. Tyagi, A. K. Prasad, J. Wengel, T C. E. Olsen and P. M. Boll. (1997). Phytochemistry of the genus Piper. Phytochemistry, 46, (4); 591-673.

Pereira B. D. and D. J. Mourab. (2008). Evaluation of the genotoxicity of piplartine, an alkamide of *Piper tuberculatum*, in yeast and mammalian V.79 cells. Mutation Research, 652: 164–174.

Pérez I, Y. S., Vidal, T. M. C., Machado, Y. A., Pelier, L. C., Navarro, G. B., & Pérez, O. P. (2015). Composición química del aceite esencial de Piper hispidum Sw. y actividad antimicrobiana sobre *Xanthomonas albilineans* (Ashby) Dowson y *Xanthomonas campestris* pv. campestris (Pammel) Dowson. *Revista de Protección Vegetal*, *29*(3), 185.

Pérez-Arellano, J. L., Cabrera, M. H., Pisos-Álamo, E., & Rodríguez, C. C. (2007). Tratamiento de las enfermedades parasitarias (I): Protozoosis. Información Terapéutica del Sistema Nacional de Salud, 31(1), 3-16.

Pessini, G. L., Dias Filho, B. P., Nakamura, C. V., & Cortez, D. A. G. (2003). Antibacterial activity of extracts and neolignans from Piper regnellii (Miq.) C. DC. var. pallescens (C. DC.) Yunck. Memórias do Instituto Oswaldo Cruz, 98(8), 1115-1120.

Pineda, M. R., S. Vizcaíno P., C. M. Garcia P., J. H. Gil G. and D. Durando R. (2012). Chemical composition and antifungal activity of Piper auritum Kunth and Piper holtonii C. DC. against phytopathogenic fungi. *Chilean Journal of Agricultural Research*, *72*, 4.

Pino, O., Sánchez, Y., Rodríguez, H., Correa, T. M., Demedio, J., & Sanabria, J. L. (2011). Caracterización química y actividad acaricida del aceite esencial de Piper aduncum subsp. ossanum frente a Varroa destructor. *Revista de Protección Vegetal*, *26*(1), 52-61.

Quijano-Abril, M. A., R. Callejas-Posada y D.R. Miranda-Esquivel. (2006). Areas of endemism and distribution patter for neotropical *Piper* species (Piperaceae) Journal of Biogeography (J. Biogeogr.) 33, 1266–1278

Quirós, M. B., Peres, N. A., & Arauz, L. F. (2013). Presencia de Colletotrichum acutatum y Colletotrichum gloeosporioides en helecho hoja de cuero, limón criollo, papaya, carambola y mango en Costa Rica y Florida (Estados Unidos). *Agronomía Costarricense*, *37*(1).

Rafael, M. S., W. J. Hereira-Rojas, J. J. Roper, S. M. Nunomura and W. P. Tadai. (2008). Potential control of *Aedes aegypti* (Diptera: Culicidae) with *Piper aduncum* L. (Piperaceae) extracts demonstrated by chromosomal biomarkers and toxic effects on interphase nuclei. Genetics and Molecular Research 7 (3): 772-781.

Ramos, G., P. Frutos, F.J. Giráldez y A.R. Mantecón. (1998). Los compuestos secundarios de las plantas en la nutrición de los herbívoros. Arch. Zootec. 47: 597-650.

Regasini, L. O., F. Cotinguiba, A. A. Morandim, M. J. Kato, L. Scorzoni, M. J. Mendes-Giannini, V. S. Bolzani and M. Furlan. (2009). Antimicrobial activity of *Piper arboreum* and *Piper tuberculatum* (Piperaceae) against opportunistic yeasts. African Journal of Biotechnology 8 (12): 2866-2870.

Rodrigues-Silva D., E. Harue Endo, B. P. Dias Filho, C. Vetaru Nakamura, T. I. Estivaleti Svidzinski, A. de Sousa, M. C. M. Young, T. Ueda-Nakamura and D. A. García Cortez. (2009). Chemical composition and antimicrobial properties of *Piper ovatum* Valh. Molecules. 14; 1171-1182.

Rodrigues-Silva, D., Nakamura, C. V., Dias Filho, B. P., Ueda-Nakamura, T., & Cortez, D. A. G. (2009). In vitro antileishmanial activity of hydroalcoholic extract, fractions, and compounds isolated from leaves of *Piper ovatum* Vahl against Leishmania amazonensis. *Acta Protozoologica*, *48*(1), 73.

Ruiz, S. P., Anjos, M. M. D., Carrara, V. S., deLima, J. N., Cortez, D. A. G., Nakamura, T. U and Abreu Filho, B. A. (2013). Evaluation of the antibacterial activity of Piperaceae extracts and nisin on Alicyclobacillus Acidoterrestris. *Journal of food science*, *78*(11), M1772-M1777.

Sanabria L., E. A. Segovia, N. Gonzales, P. Alcaraz V. D. Bilbao. (2009). Actividad larvicida de extractos vegetales acuosos en larvas de *Aedes aegypti* (primeros ensayos). Mem. Inst. Investig. Cienc. Salud, Vol. 7(2): 26-31.

Sánchez, Y., Correa, T. M., Abreu, Y., & Pino, O. (2013). Efecto del aceite esencial de *Piper auritum* Kunth y sus componentes sobre *Xanthomonas albilineans* (Ashby) Dowson y *Xanthomonas campestris pv. campestris* (Pammel) Dowson. *Revista de Protección Vegetal*, *28*(3), 204-210.

Sánchez, Y., Correa, T. M., Abreu, Y., Martínez, B., Duarte, Y., & Pino, O. (2011). Caracterización química y actividad antimicrobiana del aceite esencial de *Piper marginatum* Jacq. *Revista de Protección Vegetal*, *26*(3), 170-176.

Sánchez, Y., Correa, T. M., Abreu, Y., Martínez, B., Duarte, Y., & Pino, O. (2011). Caracterización química y actividad antimicrobiana del aceite esencial de *Piper marginatum* Jacq. *Revista de Protección Vegetal*, *26*(3), 170-176.

Sánchez, Y., Pino, O., Correa, T. M., Naranjo, E., & Iglesia, A. (2009). Estudio químico y microbiológico del aceite esencial de Piper auritum Kunth (caisimón de anís). *Revista de protección vegetal*, *24*(1), 39-46.

Sauter, I. P., Rossa, G. E., Lucas, A. M., Cibulski, S. P., Roehe, P. M., da Silva, L. A. A and von Poser, G. L. (2012). Chemical composition and amoebicidal activity of Piper hispidinervum (Piperaceae) essential oil. *Industrial Crops and Products*, *40*, 292-295.

Sawangjaroen, N., Sawangjaroen, K., & Poonpanang, P. (2004). Effects of Piper longum fruit, Piper sarmentosum root and Quercus infectoria nut gall on caecal amoebiasis in mice. *Journal of Ethnopharmacology*, *91*(2), 357-360.

Scodro, R. B. L., Pires, C. T. A., Carrara, V. S., Lemos, C. O. T., Cardozo-Filho, L., Souza, V. A. and Cortez, D. A. G. (2013). Anti-tuberculosis neolignans from Piper regnellii. *Phytomedicine*, *20*(7), 600-604.

Scott M. I., E. Puniani, H. Jensen, J. F. Livesay, L. Poveda, P. Sánchez,-Vindas, T. Durst and J. T. Arnason. (2005). Analysis of Piperaceae germplasm by HPLC and LCMS: a method for insolating and identifying unsaturated amides from *Piper* spp extracts. *J. Agri. Food Chem*. 53: 1907-1913.

Scott, M. I., B. V. Helson, G. M. Strunz, H. Finlay, P. E. Sánchez-Vindas, L. Poveda, B. J. R. Philogène and J. T. Arnason. (2007). Efficacy of Piper nigrum (Piperaceae) extract for control of insect defoliators of forest and ornamental trees. Can. Entomol. 139: 513-522.

Scott, IM. N. Gagnon, L. Lesage, B. J. R. Philogène and J. T. Arnanson. (2005). Efficacy of botanical insecticides from *Piper* species (Piperaceae) extracts for control of European chafer (Coleoptera: Scarabinae). Journal of Economic Entomology vol. 98. (3); 845-855.

Scott, M. I., H. Jesen, R. Nicol, L. Lesage, R. Bradbury, P. Sánchez-Vindas, L. Poveda, J. T. Arnason and B. J. R. Philogène. (2004). Efficacy of *Piper* (Piperaceae) extracts for control of common home and garden insect pest. J, Econ. Entomol. 97(4); 1390-1403.

Scott, M. I., H. R. Jesen, B. J. R. Philoge and J. T. Arnason. (2008). A review of *Piper* spp. (Piperaceae) phytochemistry, insecticidal activity and mode of action. Phytochem Rev 7:65–75.

Scott, M. I., N. Gagnon, L. Lesage, B. J. R. Philogène and J. T. Arnason. (2005). Efficacy of *Piper* (Piperaceae) extracts for control of common home and garden insects. Journal of Economic Entomology 97(4); 1390-1403.

Sengonca, C., Liu, B., & Zhu, Y. J. (2006). Insecticidal activity and antifeedant effect of a new type biocide GCSC-BtA against *Plutella xylostella* L.(Lep., Plutellidae). Journal of pest science, 79(1), 3-8.

Sepúlveda-Jiménez G., H. Porta-Duconing y M. Rocha-Sosa. (2003). La participación de los metabolitos secundarios en la defensa de las plantas. Revista Mexicana de Fitopatología 21(3): 355 – 363.

Shaba, P., Pandey, N. N., Sharma, O. P., Rao, J. R., & Singh, R. K. (2012). Anti-trypanosomal activity of *Piper nigrum* L (Black pepper) against Trypanosoma evansi. *J. Vet. Adv*, *2*(4), 161-167.

Silva, J. L., Souza, P. E., Monteiro, F. P., Freitas, M. L. O., Júnior, S., & Belan, L. L. (2014). Antifungal activity using medicinal plant extracts against pathogens of coffee tree. *Revista Brasileira de Plantas Medicinais*, *16*(3), 539-544.

Silva, M. L. A., Coimbra, H. S., Pereira, A. C., Almeida, V. A., Lima, T. C., Costa, E. S. & Bastos, J. K. (2007). Evaluation of *Piper cubeba* extract,(-)-cubebin and its semi-synthetic derivatives against oral pathogens. *Phytotherapy Research*, *21*(5), 420-422.

Singha, I. M. Y. Kakoty, B. G. Unni, M. C. Kañita, J. Das, A. Naglot, S. Borsingh Wan and L. Singh. (2011). Control of Fusarium wilt of tomato caused by *Fusarium oxysporum f. sp. lycopersici* using leaf extract of *Piper betle* L.: a preliminary study. World J Microbiol Biotechnol 27: 2583–2589.

Soberon, G. V., C. Rojas, J. Saavedra, M. J. Kato y G. E. Delgado. (2006). Acción biocidad de plantas de *Piper tuberculatum* Jacq. sobre *Diatrea saccharalis* (Lepidóptera, Pyralidae). Rev. Peru. Biol. 13(1):107-112.

Spring, K. y T. M. Kutchan. (2009). Chapter 1. Introduction to the Different class of Natural Products. Plant-derived Natural Products, synthesis, function and application. Spring Science-Business. USA. 3-50 p.

Sudrik, S., S. Fegade and M. Shide. (2012). Anthelmintic activity of *Piper betle* Linn, (Pann/ Nagavalli) aqueous ectract. RJPBCS 3(4) 467-470.

Taiz, L., E. Zeiger. (2010). Plant physiology. Fifth Edition. Sinauer Associates. USA. 672 P.

Tavares, W. S., I. Cruz, F. Petacci, S. S. Freitas, J. E. Serrão and J. C. Zanuncio. (2011). Insecticide activity of piperine: Toxicity to eggs of *Spodoptera frugiperda* (Lepidoptera: Noctuidae) and *Diatraea saccharalis* (Lepidoptera: Pyralidae) and phytotoxicity on several vegetables. Journal of Medicinal Plants Research Vol. 5 (21): 5301-5306.

Torres-Pelayo, V. R., Ma. S. Fernández, O. Carmona-Hernández, J. Molina-Torres and J. A. Lozada-García. (2014). A Phytochemical and Ethno-pharmacological Review of the genus Piper: As a Potent Bio-insecticide. Research Journal of Biology, 2: 104 – 114

Vinueza, S., Crozzoli, R., & Perichi, G. (2006). Evaluación in vitro de extractos acuosos de plantas para el control del nemátodo agallador Meloidogyne incognita. Fitopatol. Venez, 19, 26-31.

Wanke, S., Jaramillo, M. A., Borsch, T., Samain, M. S., Quandt, D., & Neinhuis, C. (2007). Evolution of Piperales—matK gene and trnK intron sequence data reveal lineage specific resolution contrast. Molecular phylogenetics and evolution, 42(2), 477-497.

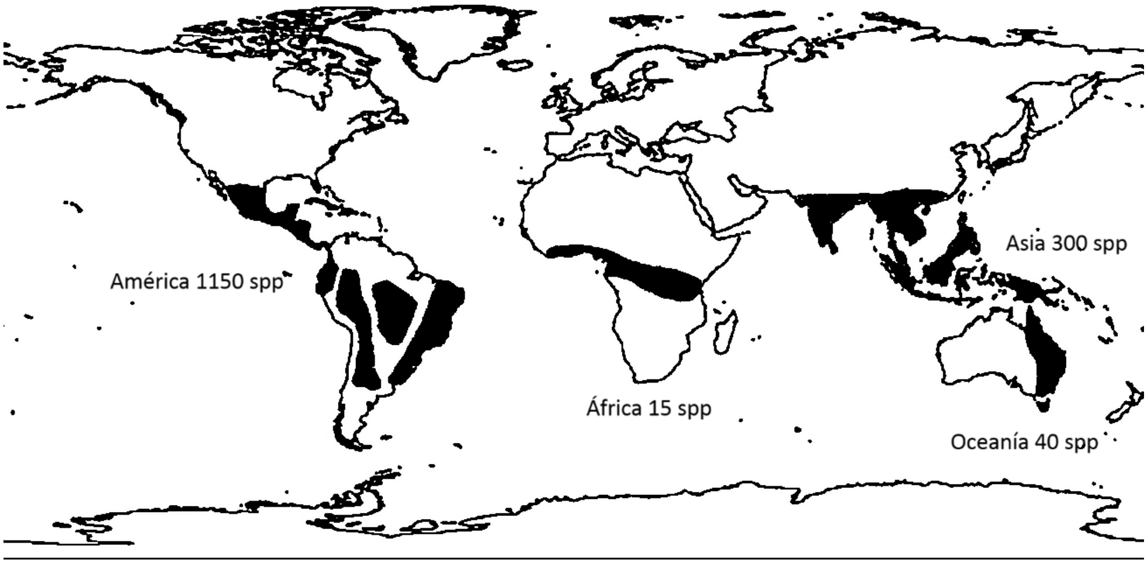
Wink, M. (2010). Chapter 1: Introdution: biochesmitry, physiology and ecological functions of secondary metabiolites. Biochesmistry of Plant Secondary Metabolites.Second Edition. Wiley-Blackwell. 1-19 p.

Wiratno, D., Taniwiryono, H. Van den Berg, J.A.G. Riksen, I.M.C.M. Rietjens, S.R. Djiwanti, J.E. Kammenga and A.J. Murk. (2009). Nematicidal Activity of Plant Etracts Against the Root-Knot Nematode, *Meloidogyne incognita*. The Open *Natural Products Journal*, 2: 77-85.

Yung-chien, T., X Nianhe and M. G. Gilbert. (1999). Flora of China 4. 110-131.

Zaidi, S. F. H., Yamada, K., Kadowaki, M., Usmanghani, K., & Sugiyama, T. (2009). Bactericidal activity of medicinal plants, employed for the treatment of gastrointestinal ailments, against Helicobacter pylori. *Journal of ethnopharmacology*, *121*(2), 286-291.

Zakaria, Z., Sreenivasan, S., & Mohamad, M. (2007). Antimicrobial activity of *Piper ribesoides* root extract against *Staphylococcus aureus*. Journal of Applied Biological Sciences, 1(3), 87-90.



Picture 1. Geographical distribution of *Piper* genus and its main diversification centers. (Based on Jaramillo and Manos, 2001).

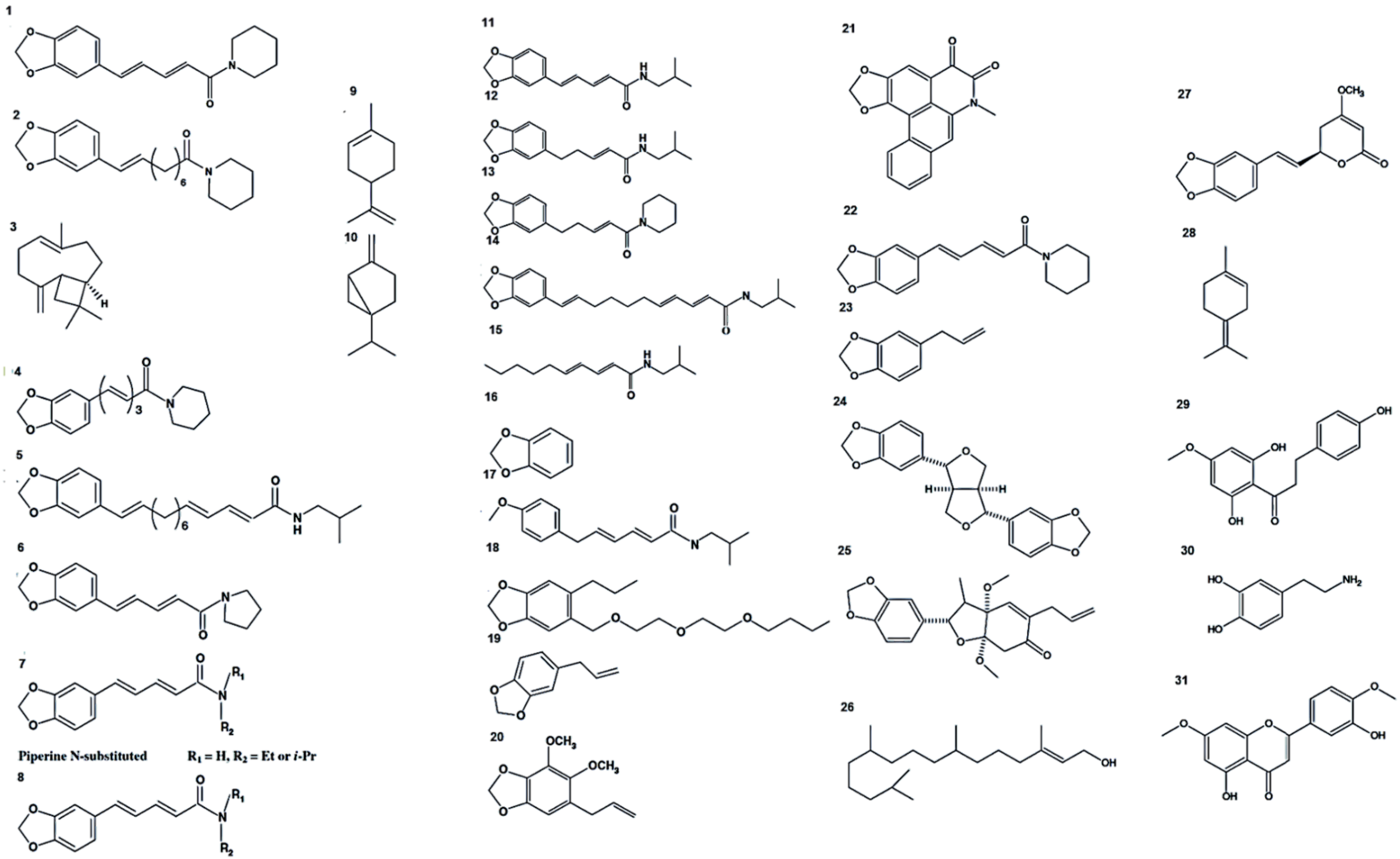


Figure 2. Structure of principal *Piper* secondary compouds: piperine (1); piperolein B (2); b-caryophyllene (3); piperlonguminine (4); dihydropiperlonguminine (5); dihydropiperine (6); pipercide (7); pellitorine (8); limonene (9); sabinene (10); guineensine (11); piperiline (12); N-substituted amides (13); N, N-disubstituted amides (14); methylenedioxyphenyl group (15); piperovatine (16); piperonyl butoxide (17); safrole (18); dillapiol (19); piperettine (20); cepharadione A (21) (22); Propenylphenol: safrole (23); Lignan: sesamin (24); Neolignan: kadsurin A (25); Terpenes: transphytol (26), terpinolene (27); Kawapyrone: methysticin (28); Dihydrochalcone: asebogenin (29); Other: dopamine (30); Flavone: 7,4'-dimethoxy-5,3'-dihydroxyflavone (31). (Take of Scott *et al*., 2008 and Dyer *et al*., 2004)

Table 1. Organisms where *Piper* L. has had activity

Piper spices	Organisms evaluates	Species	Bioactivity	References
P. brachypodom, P. auritum, P. cf. divaricatum, P. bredemeyeri, P. eriopodon, P. septuplinervium, P. marginatum, P. laceifolium, P. bogotense	Arthropods	*Artemia franciscana,*	Toxicity	Olvero-Verdel, *et al*., 2009:
P. aduncum, P. auritum, P. longum, P. ribesoides, P. sarmentosum		*Aedes egypti,*	Insecticide	Choochote *et al*., 2006, Leyva *et al*., 2009; Misni *et al*., 2008; Rafael *et al*., 2008
P. nigrum, P. tuberculatum, P. guineense		*Malacosoma americanum,*	Insecticide	Scott *et al*., 2004
P. nigrum, P. guineense, P. tuberculatum		*Neodiprion sertifer*	Insecticide	Celis *et al*., 2008; Scott *et al*., 2004
P. aduncum, P. nigrum		*Musca domestica*	Insecticide y Repelente	Kong *et al*., 2009; Jensen *et al*., 2006;
P. nigrum, P. grande, P. aduncum, P. amalago, P. hispidum, P. psilorhachis, P. diandrum, P. sanctum, P. nudum, P. auritum, P. umbellatum		*Drosophila melanogaster*	Insecticide	Jensen *et al*., 2006, Jensen *et al*., 2005; Granados *et al*., 2002; Carmona-Hernández *et al*., 2014

P. crassinervium, P. aequale P. amalago, P. xylosteoides, P. makanianum		*Rhipicephalus (Boophilus) microplus*	Insecticide	Garcia-Paz, 2011, Ferraz *et al*., 2010
P. nigrum, P. tuberculatum,		*Diatrea saccharalis*	Insecticide	Tavares *et al*., 2011; Soberón *et al*., 2006
P. eriopodon, P. umbellatum, P. pesaresanum		*Hyphothenemus hampei*	Insecticide	Mosquera *et al*., 2009
P. guineense		*Sitophilus zeamais*	Insecticide	Asawalam, 2006
P. nigrum		*Spodoptera frugiperda*	Insecticide	Tavares *et al*., 2011
P. auritum		*Spodoptera exigua*	Entomotóxica	Delgado Barreto *et al*., 2012
P. aduncum		*Varroa destructor*	Acaricida	Pino *et al*., 2011
P. betel, P. nigrum, P. marginatum	Nematicide and anthelmintic	*Meloidogyne incognita*	Nematicida y Anthelmintic	Dammanini Premanchandra *et al*., 2014 Wiratno *et al*., 2009; Vinueza *et al*., 2006
P. betel, P. nigrum		*Caenorhabditis elegans*	Nematicide y anthelmintic	Evans *et al*., 1984; Atjanasuppat *et al*., 2009
P. betel		*Eisenia fetida*	Anthelmintic	Sudrik *et al*., 2012
P. aduncum		*Haemoncus contustus*	Anthelmintic	Lopes-Oliveira *et al*., 2014
P. nigrum, P. longum		*Pheretima posthuma*	Anthelmintic	Devi *et al*., 2011
P. nigrum		*Tridax procumbens*	Anthelmintic	Ashish Patiland Annasaheb Niyave., 2014

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P. nigrum, P. cubeba P. chaba		*Schistosoma mansoni*	Anthelmintic	Atjanasuppat *et al*., 2009; Magalhães *et al*., 2011
P. betle	Funguses	*Fusarium oxysporum*	Fungicide	Sigha *et al*.,2011
P. betel, P. tuberculatum		*Microsporum gypseum*	Fungicide	Intzar *et al*., 2010; Palacios *et al*., 2009
P. betel, P. tuberculatum		*Microsporum canis*	Fungicide	Intzar *et al*., 2010; Palacios *et al*., 2009
P. betel, P. tuberculatum		*Trichophyton rubrum*	Fungicide	Intzar *et al*., 2010; Palacios *et al*., 2009
P. betel, P.sanctifelis, P. auritum, P. aduncum		*Apergillus flavus*	Fungicide	Intzar *et al*., 2010; Mesa *et al*., 2007
P. betel, P.sanctifelis, P. auritum, P. aduncum		*Aspergillus fumigatus*	Fungicide	Intzar *et al*., 2010; Mesa *et al*., 2007
P. nigrum		*Aspergillus* sp	Fungicide	Akthar *et al*., 2014
P. betel, P. ovatum, P.sanctifelis, P. auritum, P. aduncu, P. amalago, P. cernun, P. diospyrifolium, P. Crassinervium, P. gaudichaudianum, P. Solmsianum, P. Regnallii, P. tuberculatum.P. tuberculatum		*Candida krusei,*	Fungicide	Intzar *et al*., 2010; Rodrigues-Silva *et al*., 2009; Morandim-Giannetti *et al*., 2010; Regasini *et al*., 2009.
P. betel, P. ovatum P.sanctifelis, P. auritum, P. aduncum, P. amalago, P. cernun, P.		*Candida parapsilosis*	Fungicide	Intzar *et al*., 2010; Rodrigues-Silva *et al*., 2009; Morandim-Giannetti *et al*.,

diospyrifolium, P. Crassinervium, P. gaudichaudianum, P. Solmsianum, P. Regnallii, P. tuberculatum.P. arboreum				2010: Regasini *et al*., 2009.
P. betel, P. ovatum, P. tuberculatum.P. arboretum, P. nigrum		*Candida albicans*	Fungicide	Intzar *et al*., 2010; Rodrigues-Silva *et al*., 2009: Regasini *et al*., 2009; Akthar *et al*., 2014
P. ovatum		*Candida tropicalis*	Fungicide	Rodrigues-Silva *et al*., 2009
P. ovatum		*Candida glabrata*	Fungicide	Rodrigues-Silva *et al*., 2009
P. auritum, P. holtonii		*Botryodiplodia theobromae*	Fungicide	Pineda at al., 2012
P. auritum, P. holtonii		*Colletotrichum acutatum*	Fungicide	Pineda at al., 2012
P. auritum, P. holtonii		*Colletotrichum gloeosporioides,*	Fungicide	Pineda at al., 2012
P. aduncum, P. auritum		*Curvularia lunata*	Fungicide	Duarte *et al*. 2014
P. aduncum, P. auritum		*Sarocladium oryzae*	Fungicide	Duarte *et al*. 2014
P. aduncum, P. auritum		*Bipolaris oryzae*	Fungicide	Duarte *et al*. 2014
P. longum, P. sarmentosum	Protozoans	*Entamoeba histolytica*	Antiamoebic	Ghoshal *et al*., 1996; Sawangjaroen *et al*., 2004
P. ovatum, P. amalago		*Leishmania amazonensis*	Antileishmanial	Rodriguez-Silva *et al*., 2009, Carrara *et al*., 2013

P. nigrum		*Trypanosoma evansi*	Antitripanosomal	Shaba *et al*., 2012
P. hispidinrvum		*Acanthamoeba polyphaga*	Antiamoebic	Sauter *et al*., 2012
P. betel	Bacteria	*Streptococcus pyogenes,*	Bactericide	Chakraborty and Shah, 2011,
P. cubeba		*Streptococcus salivarius*	Bactericide	Silva *et al*., 2007
P. cubeba		*Streptococcus mutans*	Bactericide	Silva *et al*., 2007
P. cubeba		*Streptococcus sanguinis*	Bactericide	Silva *et al*., 2007
P. cubeba		*Streptococcus mitis*	Bactericide	Silva *et al*., 2007
P. betel, P. ovatum, P. porphyrophyllum, P. nigrum, P.r regnellii, P. aduncum		*Staphylococcus aureus,*	Bactericide	Chakranorty and Shah, 2011, Rodrigues-Silva *et al*., 2009; Benítez *et al* ., 2009; Ahmmad *et al*., 2014; Akthar *et al*., 2014; Arani Datta *et al*., 2011; Karsha and Lakshme, 2010; Brazao *et al*., 2014, Pessini *et al*., 2003

P. betel		*Proteus vulgaris,*	Bactericide	Chakraborty and Shah, 2011; Arani Datta *et al*., 2011
P. betel, P. ovatum; P. lanceifolium, P. porphyrophyllum, P. nigrum, P. regnellii		*Escherichia coli*	Bactericide	Chakraborty and Shah, 2011; Rodrigues-Silva *et al*., 2009; Benítez *et al*., 2009; Akthar *et al*., 2014; Karsha and Lakshme, 2010, Pessini *et al*., 2003
P. ovatum, P. lanceifolium, P. regnellii		*Bacillus subtilis*	Bactericide	Rodrigues-Silva *et al*., 2009; Benítez *et al*., 2009, Pessini *et al*., 2003
P. nigrum		*Bacillus cerus*	Bactericide	Karsha and Lakshme, 2010
P. lanceifolium, P. nigrum		*Salmonella tiphy*	Bactericide	Benítez *et al*., 2009: Karsha and Lakshme, 2010
P. nigrum		*Salmonella typhimurium*	Bactericide	Akthar *et al*., 2014
P. lanceifolium; P. betel, P. nigrum		*Klebsiella pneumoniae*	Bactericide	Benítez *et al*., 2009; Arani Datta *et al*., 2011; Karsha and Lakshme, 2010

P. lanceifolium, P. porphyrophyllum, P. betel P. regnellii, P. nigrum		*Pseudomona aeruginosa*	Bactericida	Benítez *et al.*, 2009; Akthar *et al.*, 2014; Datta *et al.*, 2011; Pessini *et al.*, 2003: Karsha and Lakshme, 2010, Pessini *et al.*, 2003
P. aduncum		*Staphylococcus lentus*	Bactericida	Brazao *et al.*, 2014
P. ovatum, P. aduncum		*Staphylococcus epidermis*	Bactericida	Rodrigues-Silva *et al.*, 2009; Brazao *et al.*, 2014
P. ovatum		*Enterobacter cloaceae*	Bactericida	Rodrigues-Silva *et al.*, 2009
P. aduncum, P. amalago, P. arboderum, P. crassinervium, P. hispidum, P. xylosteoides		*Alicyclobacillus acidoterrestris*	Bactericida	Ruiz *et al.*, 2013
P. cubeba, P. nigrum		*Enterococcus faecalis*	Bactericida	Silva *et al.*, 2007: Karsha and Lakshme, 2010
P. cubeba, P. nigrum, P. longum		*Helicobacter pilory*	Bactericida	Zaidi *et al.*, 2009
P. regnellii		*Mycobacterium tuberculosis*	Antituberculosis	Scodro *et al.*, 2013

P. marginatum, P. hispidum		*Xanthomonas albilineas*	Antimicrobiana	Sánchez *et al.*, 2011, Sánchez *et al.*, 2014
P. marginatum, P. hispidum		*Xanthomonas campestris*	Antimicrobiana	Sánchez *et al.*, 2011, Sánchez *et al.*, 2014