UNIVERSIDAD DE INVESTIGACIÓN DE TECNOLOGÍA EXPERIMENTAL YACHAY

Escuela de Ciencias Biológicas e Ingeniería

TÍTULO: Review of anti-inflammatory activity and chemical composition of *Muehlenbeckia tamnifolia, Baccharis latifolia, Senecio canescens, and Cestrum peruvianum* native plants to Ecuador

Trabajo de integración curricular presentado
como requisito para la obtención
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Autora:
Sangurima Paute Verónica Adriana

Tutor:
Ph.D. Gudiño Gomezjurado Marco Esteban

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Estudiante

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Presidente Tribunal de Defensa

Dr. GUDIÑO GOMEZJURADO, MARCO ESTEBAN , Ph.D.
Tutor

Dra. LIRA VERGARA RENE CONSTANZA , Ph.D.
Miembro No Tutor

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Dedicatoria

A mis padres que siempre estuvieron a mi lado apoyándome y sentaron en mí las bases de una persona feliz con lo que hace. A mis queridas hermanas Eli, Cati, y hermanos Fabi y Manchis que me ayudaron con sus consejos y apoyo moral para no abandonar mis sueños. Además, a mis grandes amigas Pola y Gine que me acompañaron a enfrentar mis miedos y me respaldaron en mi vida universitaria.

Verónica Adriana Sangurima Paute

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Verónica Adriana Sangurima Paute

Resumen

A nivel mundial hay una gran cantidad de recursos naturales que han sido utilizados desde la antigüedad, generalmente las personas que las utilizan lo hacen por conocimiento adquirido desde generaciones anteriores. Las plantas están compuestas por un sinnúmero de compuestos bioactivos siendo los metabolitos secundarios o fitoquímicos los que mayor potencial tienen por sus propiedades químicas. Los fitoquímicos pueden clasificar en fenoles, terpenoides o terpenos, compuestos oranosulfurados, y alcaloides los cuales por sus características químicas son relevantes para contrarrestar actividad microbiana, antiinflamatoria, antioxidante, antiviral entre otras. Específicamente el proceso inflamatorio está caracterizado por ser un proceso que busca la homeostasis del cuerpo humano después de sufrir de la intervención de agentes infecciosos o no infecciosos. En el ecuador hay plantas nativas como muehlenbeckia tamnifolia, baccharis latifolia, senecio canescens, y cestrum peruvianum constituidas por fitoquímicos que presentan potencial para contrarrestar la actividad antiinflamatoria. Finalmente, es necesario reconocer los tipos de métodos para la extracción, aislamiento y análisis de los fitoquímicos en las plantas.

Key words: fitoquimicos, proceso antiinflamatorio, Ecuador, etnomedicina.

Abstract

Worldwide, there are many natural resources used since ancient times; generally, people use plants by knowledge acquired from previous generations. Plants are made up of countless bioactive compounds, the secondary metabolites or phytochemicals being the ones with the most significant potential due to their chemical properties. Phytochemicals can be classified into phenols, terpenoids or terpenes, organosulfur compounds, and alkaloids. Their chemical characteristics are relevant to counteract microbial, anti-inflammatory, anti-oxidant, and anti-viral activity. Specifically, the inflammatory process is characterized by being a process to maintain the homeostasis of the human body after suffering from the intervention of infectious or non-infectious agents. in Ecuador, there are native plants such as *Muehlenbeckia tamnifolia, Baccharis latifolia, Senecio canescens, and Cestrum peruvianum* with phytochemicals with the potential to counteract anti-inflammatory activity. Finally, it is necessary to recognize the methods for the extraction, isolation, and analysis of phytochemicals in plants.

Key words: phytochemicals. Ecuador, anti-inflammatory properties, etnomedicine.

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Chapter I

1. Introduction

Plants are elements with important chemical properties to counteract the inflammatory process in the human body. Since ancient times, plants have been a source to treat different types of ailments such as inflammation, headache, dislocations, fever, hernias, stomach pain, among others; in general, rural communities use plants to treat different ailments because previous generations have experienced through success and failure the usefulness of a particular plant, knowledge transmitted orally. Ethnomedicine or traditional medicine encompasses empirical knowledge about valuable plants that are not scientifically determined. Ecuador is a mega-diverse country with countless species both in fauna and flora. Guevara et al. (1) report that the Ecuadorian Amazon is one of the most biodiverse regions on Earth. Ecuador has many native plants with anti-oxidant, anti-microbial, anti-cancer potential, particularly facing the anti-inflammatory process.

Plants are organisms that interact with the environment, constituted by primary and secondary metabolites. The primary metabolites are the elements necessary for the plant's sustenance; although secondary metabolites do not execute vital functions in the development of the plant, their chemical properties can positively intervene in anti-oxidant, anti-microbial, anti-cancer potential, and the anti-inflammatory process. Secondary metabolites can be classified as terpenoids, phenolic compounds, alkaloids, and sulfur-containing compounds (2). *Muehlenbeckia tamnifolia, Baccharis latifolia, Senecio canescens, and Cestrum peruvianum* are native plants spread from southern Mexico to Argentina. The traditional use of these plants by the population is for sprains, abdominal pain, menstrual pain, and headaches. All these plants present phytochemicals or secondary metabolites.

On the other hand, inflammation is a natural defense mechanism for eliminating harmful invaders such as viruses or bacteria; and cells do not fulfill the established functions. The anti-inflammatory process through different molecules and cellule y mechanisms starts the healing process (3). Overall, inflammation is classified into acute inflammation that is rapid response; or chronic in response when acute inflammation does not resolve (4). There is research to determine the types of elements and their chemical characteristics in these native Ecuadorian plants. For the extraction of phytochemicals, called conventional and advanced methods are used. Likewise, the chromatography method is used to isolate phytochemicals, and a spectrometry method is a valuable tool for the analysis of phytochemicals. This review performs a collection of information about the secondary metabolites or phytochemicals that present *Muehlenbeckia tamnifolia, Baccharis latifolia, Senecio canescens, and Cestrum peruvianum a*nd their relationship with anti-inflammatory properties.

Chapter II

2. Problem situation

The pharmaceutics field always is facing significant challenges in developing new compounds to satisfy the necessities in the inflammatory processes. According to Yuan et al. (5) there is evidence of plants' use like medicines in fossil registries ago 60,000 years on the part of the human. Similarly, it has been recorded that the pharmaceutical industry contains around 25% of medicines from plants (6,7), and more than twelve thousand phytochemicals have been isolated from various plants, such as flavonoids from fruits, isoflavones from soybeans, and lycopene from tomatoes until 2018 (8). Consequently, now has been attention to the search alternatives of both natural and synthetic origin to contribute to new drugs. The native natural products of Ecuador are products that have countless compounds with a broad chemical diversity. Although native plant compounds from Ecuador are being investigated, the existing information on phytochemicals and their anti-inflammatory properties is limited. Therefore, it is necessary to compose a compilation of information on the phytochemicals, chemical properties, and anti-inflammatory activity of *Muehlenbeckia tamnifolia, Baccharis latifolia, Senecio canescens, and Cestrum peruvianum* Ecuadorian native plants because this information could be the basis of interest for scientific research, and allow to verify the relationship between phytochemicals and anti-inflammatory properties, and finally contribute to the development of the pharmaceutical field.

2.1. Problem formulation

To give visualization in the scientific field to a certain group of native Ecuadorian plants that contribute to the development of drugs, it is relevant to establish the following question:

How native plants of Ecuador such as *Muehlenbeckia tamnifolia, Baccharis latifolia, Senecio canescens, y Cestrum peruvianum* are related to anti-inflammatory properties?

2.1.1. Research justification

Plants are in continuous contact with humans since ancient times. It is estimated more than 500,000 species are part of the world's plant diversity, and around 150,000 plant species contain valuable therapeutic agents, and the number of plants bioactive for pharmaceutical purposes is gradually increasing in recent years (9). Besides, plants are considered true living chemical factories for the biosynthesis of a wide variety of secondary metabolites (SM). Thus, the Plant Kingdom encompasses botanical elements containing phytochemicals identified as a promising research target searching for new pharmaceutical compounds to counteract several diseases (10,11). To illustrate, it is necessary to indicate that plants are a source of some anti-inflammatory drugs (7). Rodríguez et al. (12), reported that *Muehlenbeckia tamnifolia* demonstrated an anti-inflammatory effect in an animal model. As well, Ecuador is a mega-diverse country with countless native plants not threatened with pharmaceutically active secondary metabolites to counteract ailments; even so, they have not been thoroughly investigated. Therefore, compiling bibliographic information covering the phytochemical characteristics like *Muehlenbeckia tamnifolia, Baccharis latifolia, Senecio canescens, y Cestrum peruvianum* native plants of Ecuador with important chemical characteristics allow giving a visualization of these botanical resources to the pharmaceutical field.

2.2. Objective

2.2.1. General objective

To review of anti-inflammatory activity and chemical composition of *Muehlenbeckia tamnifolia, Baccharis latifolia, Senecio canescens, y Cestrum peruvianum* native plants of Ecuador to development of drugs.

2.2.2. Specific objectives

i. To describe the traditional uses of *Muehlenbeckia tamnifolia, Baccharis latifolia, Senecio canescens and Cestrum peruvianum* focused as source to primary health care.
ii. To describe the botanical characteristics and the geographical distribution of researched native plants.
iii. To indicate at a general level the classification, subclassification, and use in the health area of the chemical elements found in plants.
iv. To explain in a general way about the inflammatory, anti-inflammatory process, and studies about the effect produced by the plants studied in inflammatory processes.
v. To describe the general aspects of the extraction, isolation, and analysis methods used in phytochemicals.

2.3. Hypothesis

Muehlenbeckia tamnifolia, Baccharis latifolia, Senecio canescens, and Cestrum peruvianum native plants of Ecuador have anti-inflammatory properties.

Chapter III

3. Ethnomedicine in Ecuador

Plants are the source of primary health care in various parts of the world (13). Since ancient times humans have used plants to counteract or minimize different types of symptoms associated with various diseases as part of the traditions or experiences established by practical way from generation to generation (14). As a result, plants' use to cure disease is deeply rooted by various indigenous groups and rural communities and is increasingly spreading to the rest of the population (15). In 2018, Souza et al. indicate that people in some areas of Brazil the medicinal plants are preferred over western ones because they are considered cheaper and have fewer adverse effects (13). Medicinal ancestral knowledge is known as Traditional Medicine or Ethnomedicine that is oral, not written, and more ethnic and less scientific **(Figure 1)** (16).

People use plants to treat different types of ailments such as inflammation, headache, dislocations, fever, hernias, and stomach pain, generally without knowing the scientific reason for the involved process. Singh Bishander et al. (17), reported that Ethnomedicine research around 5000 species of plants of different taxonomic groups to treatment people's ailments. Presently, there is a large number of traditional vegetal resources have attracted researchers' attention, as a result, there is a greater focus of the scientific community on experimentation in plants to test their bioactive efficacy and safety. Accordingly, the World Health Organization (WHO) is actively working on the collection of information on medicinal plants in the traditional folk medicine system (18).

According to "Phytochemistry and Ethnopharmacology of the Ecuadorian Flora. A Review", reported the community's Andean Ecuadorian before and after the Spanish conquest used the knowledge medical of plants to treat illness and was transmitted between generations to preserve the information. Ecuador is a mega-diverse country with countless animal and plant species; the biodiversity of Ecuador is because of the location in the center of the planet, crossed by the Andes, the Amazon basin the currents of the Pacific Ocean. Ecuador is a perfect place where human cultures have developed together with the environment (19,20). In 2016, Abril et al. reported that there are more than 400 studies related to ethnobotanical areas in Ecuador, and in the Amazonian region, there are around 100 studies in fields like general ethnobotany. Also, *Asteraceae and Fabaceae* family are more used in Ecuador to treat infections, wounds, injuries, stomach disorders (21).

3.1. Relationship between phytochemistry and botanical sources

Phytochemistry focuses on the study of chemicals produced by plants (22) known as phytochemicals. According to Malagón et al. (23), plants are used to develop medicines, as a result, are constituted by different chemical compounds with influence in the human body. In fact, Friedrich Wilhelm isolated for the first time an active ingredient associated with a medicinal plant or herb, which opened the way to promote concern regarding the chemical composition and characteristics of the elements that made up different types of plants (24). Phytochemicals have various therapeutic applications like anti-inflammatory, anti-allergic, anti-cancer, antibacterial, anti-viral, and analgesic (7). For this reason, phytochemical research has focused on covering the isolation of phytochemicals, determining their structure by spectral methods, and evaluating their biological property in both vivo and in vitro studies (Figure 1) (11). Plants synthesize a great diversity of low molecular weight organic compounds (25) classified as primary metabolites, secondary metabolites, and plant hormones (26). Therefore, the primary and secondary metabolites are chemical elements relevant to the study of photochemistry (27).

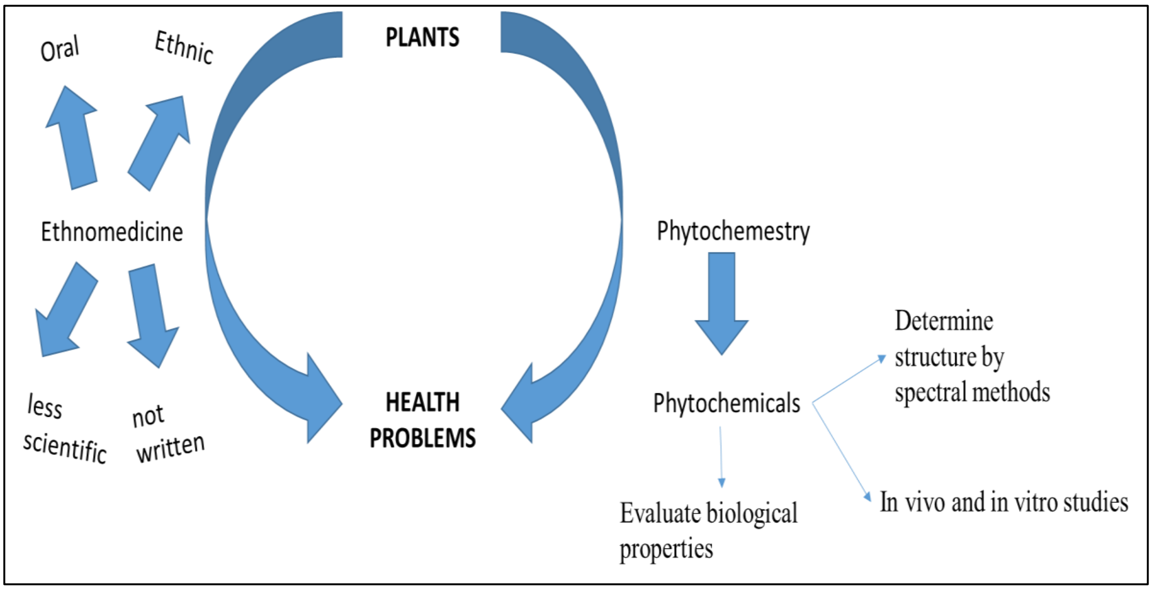

Figure 1.- Relationship between Ethnomedicine and Phytochemistry with health.

3.1.1. Primary metabolites and secondary metabolites

The metabolite is a minor substance produced during metabolism. Thirumurugan et al. (28), observed that primary metabolite are molecules similar in all living beings; classified into fats, amino acids, tricarboxylic acid, intermediates of the Krebs cycle, proteins, nucleic acids, sugars, generally produced in plant species for their essential biological function like cell division, growth, respiration, storage, and reproduction (26). Similarly, secondary plant metabolites are bioactive but non-nutritious compounds (29,30) known as phytochemicals. Secondary metabolites are found naturally in plant parts such as flowers, leaves, fruits, roots, and barks. Also, secondary metabolites are generally synthesized in the plant as a self-defense measure against insects, pests, pathogens, herbivores, ultraviolet exposure, and environmental hazards (20,22). They act as substrates for biochemical reactions, cofactors, and inhibitors in enzyme-catalyzed reactions and eliminate reactive, toxic compounds in the human body.

Secondary metabolites are particular and are found in large numbers among the various groups of plants. Secondary metabolites are classified as terpenoids, alkaloids, phenolics, and sulfur compounds (18,31). The functions and classification of metabolite primary and secondary are shown in Table 1.

Table 1.- function and examples of primary and secondary metabolite.

Metabolite	Function	Classification of metabolite	Ref
Primary	Biological functions in plants such as cell division, growth, respiration, storage, and reproduction.	Fats, amino acids, tricarboxylic acid, intermediates of the Krebs cycle, proteins, nucleic acids, and sugars.	(19)
Secondary	-In the plant to self-defense. -Bioactive compounds.	Terpenoids, alkaloids, phenolics, and sulfur compound.	(7,22,23,24)

Thirumurugan et al., in their book "Secondary Metabolites - Sources and Applications," published in 2018, explain that the plants are significant sources of secondary metabolites with around 80 percent of the total, and 20 percent result from to bacteria, fungi, and marines sources (28). Secondary metabolites form the basis of a large number of commercial pharmaceutical drugs and remedies derived from medicinal plants (32,33). As a result, the secondary metabolites are crucial to understanding certain plants' effects to resolve o minimize symptoms or diseases.

3.1.2. Phytochemicals and the pharmaceutical industry

Phytochemical from the Greek word "Phyto" means plant; therefore, phytochemicals are compounds produced by plants due to their metabolism. Some researchers indicate their investigation's relation between phytochemical and secondary metabolite; some say that secondary metabolite is equal to phytochemical. Also, phytochemicals are in higher plants and less primitive plants. Phytochemicals are natural compounds of plant origin present with pharmacological and toxicological effects both in humans and animals. In 2017, Choudhury et al. reported that around 11% of 252 medicines considered basic and essential were exclusively plants origin, according to the World Health Organization. Several plants have relevant phytochemicals in the pharmaceutical field, like colchicine (*Colchicum autumnale*), paclitaxel (*Taxus brevifolia*), artemisinin (*Artemisia annua*), quinine (*Cinchona sp*.), Morphine (*Papaver somniferum*), Capsaicin (*Capsicum annuum*), where the association of phytochemistry and pharmaceutical allow knowledge the properties of these metabolites (18).

3.2. Taxonomic classification

Table 2.- Taxonomic classification of *Baccharis latifolia, Senecio canescens, Cestrum peruvianum, and Muehlenbeckia tamnifolia.*

Kingdom	**Family**	**Species**	**Common name**	**Ref**
Plantae	Asteraceae	*Baccharis latifolia*	Chilca	(34,35)
Plantae	Asteraceae	*Senecio canescens*	Oreja de conejo	(36)
Plantae	Solanaceae	*Cestrum peruvianum*	Sauco negro	(37)
Plantae	Polygonaceae	*Muehlenbeckia tamnifolia*	Anguyuyo	(38)

Table 2 show about kingdom, family and common name of *Baccharis latifolia, Senecio canescens, Cestrum peruvianum, and Muehlenbeckia tamnifolia.*

According to Malagóna et al. in the "Catalogue of the Vascular Plants of Ecuador," there are registered 15,901 botanical species, of which 15.306 are native plants. Table 3 shows about the family of native plants of review and the number of each family, where Asteraceae family has a greater number of species than the Polygonaceae family with fewer species (23).

Table 3.- Number of plant species of every family of native plant Ecuadorian of review.

Family	Number of native plants species of Ecuador
Asteraceae	863
Solanaceae	338
Polygonaceae	31

3.3. Botanical description

3.3.1. Baccharis latifolia

Baccharis latifolia known as "chilca" in Ecuador, in other places in America is known as "chilca azul", or “chilca blanca " (39). Native shrub, with a height of 1 to 4 meters approximately. The roots are deep, conserve moisture, and are necessary when for dry weather. The stems begin their branching from the root, with a characteristic brown color, cylindrical and thin that gradually decrease in diameter. As for its branches, are green in color, have resin glands that secrete resin for the protection of external agents such as insects. The leaves are simple oval in shape with serrated edges, also, they have resin glands. The flowers are more populated at their base, have 1 to 2 rows of "small hairs" or papus on the white flowers (40).

3.3.2 Senecio canescens

Senecio canescens known as "oreja de conejo" in Ecuador, in other countries such as Peru known as "vira-vira" or "huila-huila". It is grass with a height of between 50 to 65 centimeters approximately. Senecio canescens has erect woolly stems (41). The leaves are woolly opposite caulinares. As for its flowers, has a tubular shape with a characteristic yellow color.

3.3.3. Cestrum peruvianum

Cestrum peruvianum known as “Sauco negro” in Ecuador, in Peru known as "Hierba santa". It is a woody shrub with a height of between 2 to 3 meters. The stems are thin where branches extend from the base (42). The leaves have a characteristic fetid odor. Flowers are clustered and elongated. *Cestrum peruvianum* grows wild or cultivated, to irrigation canals with sandy-textured soils and also in clay soils (43).

3.3.4. Muehlenbeckia tamnifolia

Muehlenbeckia tamnifolia known as "Anguyuyo" in Ecuador. Shrub, has branches with red terminals, its leaves are cordate, that is, in the shape of a heart, or sagittate with a diameter of 8 cm. Flowers are grouped from the same stem (42).

3.4. Ethnobotanical uses

3.4.1. Baccharis latifolia

People often boil the leaves with salt for baths with the intention of reducing joint inflammation, numbing nerves and tendons, and disinfecting wounds (39). Also, the leaves are used in infusion for stomach pain caused by exposure to cold, reduce flatulence, diseases associated with the uterus, painful periods, headaches, and toothaches. Stems and leaves are usually infusion and decoction to use as an antidiabetic tonic. Another way to use is by crushing the leaves to form a kind of soft paste called "poultice", to place in dislocations, sprains, and hernias, as the result, reduce inflammation of the affected part. The resin secreted by this plant is used to prepare patches that relieve pain from rheumatism and hernias. According to Ortuño (44), in the Ecuadorian highlands, *Baccharis latifolia* is used for inflammations, problems in the uterus; infections, and skin wounds.

3.4.2. Senecio canescens

Senecio canescens is used by a decoction of stems and leaves to counteract respiratory diseases such as bronchitis, asthma, cough. In addition, stems and leaves are used on infusion to treat nerve problems, anti-inflammatory, weakness, stomach problems, and to relieve pain (45). *Senecio canescens* is used as biocides for its repellent properties against pests and diseases in crops (46).

3.4.3. Cestrum peruvianum

Cestrum peruvianum is used to relieve many symptoms, including headache, hemorrhoids, fever, and rheumatism. The infusion of the leaves is used to cure "susto", "mal aire", and kidney problems. The leaves and flowers in infusion are used to treat fever and inflammation of the tonsils. Also, is used the hot bath to colds, externally to treat rheumatoid arthritis and prevent hair loss (47).

3.4.4. Muehlenbeckia tamnifolia

Macerated leaves *Muehlenbeckia tamnifolia* are used to treat kidney diseases and toothache. Also, the leaves are used as an infusion to relieve arthritis pain. Another use that is given is as a disinfectant and to treat purulent skin wounds. The juice of the crushed leaves is used mainly as external wound healing. The ripe leaves can be used as a remedy for influenza or menstrual cramps. It is used for wound healing and healing for gastric ulcers. In Ecuador, it is common for Andean communities to use the leaves in infusion and mixed with flaxseed to treat bumps and inflammations, headaches. In addition, the crushed leaves are used to form a paste to apply to wounds with pus (12).

Table 4.-Description of part used to traditional use of *Muehlenbeckia tamnifolia , Baccharis latifolia, Senecio canescens, Cestrum peruvianum.*

Especie	Traditional use	Parts used	Ref.
Muehlenbeckia tamnifolia	Kidney disease, bone pain, toothaches, disinfectant and menstrual cramps.	Leaves and stems.	(12,38)
Baccharis latifolia	Inflammation, dislocations, hernias, flatulence, stomach pain, fractures, wounds, and ulcers.	Leaves and, stems.	(40,48)
Senecio canescens	Respiratory infection.	Leaves and flower.	(43)
Cestrum peruvianum	Headache, hemorrhoids, and fever.	Leaves.	(37)

Table 4 explains the used parts of *Muehlenbeckia tamnifolia, Baccharis latifolia, Senecio canescens, and Cestrum peruvianum* and the traditional uses that are given to each of these botanical species.

3.5. Geographical distribution

3.5.1. Baccharis latifolia

It is distributed in areas of 2500-3600 m, adapts in soils with a small amount of organic matter and humidity; found on slopes, paddocks, roadsides (49). *Baccharis latifolia* develops in cold climates, grows spontaneously. Native shrub distributed in South America especially in the Andean zone from Colombia to the north of Argentina. In Ecuador is Andean region such as mountainous areas, streams, rivers, although is present in areas of Amazon Ecuador such as Napo and Zamora Chinchipe (39,50,51).

3.5.2. Senecio canescens

Senecio canescens extends in Andean areas at a height of 3600 to 5000 m., is in areas with grasslands. It is found in Andean areas from Venezuela to the northern region of Argentina (52).

3.5.3. Cestrum peruvianum

It is a shrub that is located in areas from 1500-4000 meters. It in tropical regions of America, it ranges from the southeastern United States to Peru. It can be found in irrigation canals, soils with a sandy or clay texture (47).

3.5.4. Muehlenbeckia tamnifolia

Muehlenbeckia tamnifolia extends in warm tropical and subtropical zones to Andean zones, at an altitude of 2000 to 5000 m. They can be found in forests, roadsides, and rocks. It can be found from Mexico to Argentina. In Ecuador, it is found in the Andean region, although, is in some provinces of the Amazon Ecuadorian such as Napo, Morona Santiago, and Zamora Chinchipe (43).

The **(Figure 2)** shows geographical location in the region American and Ecuador of *Muehlenbeckia tamnifolia, Baccharis latifolia, Senecio canescens, and Cestrum peruvianum,* and the areas where grow these plant species.

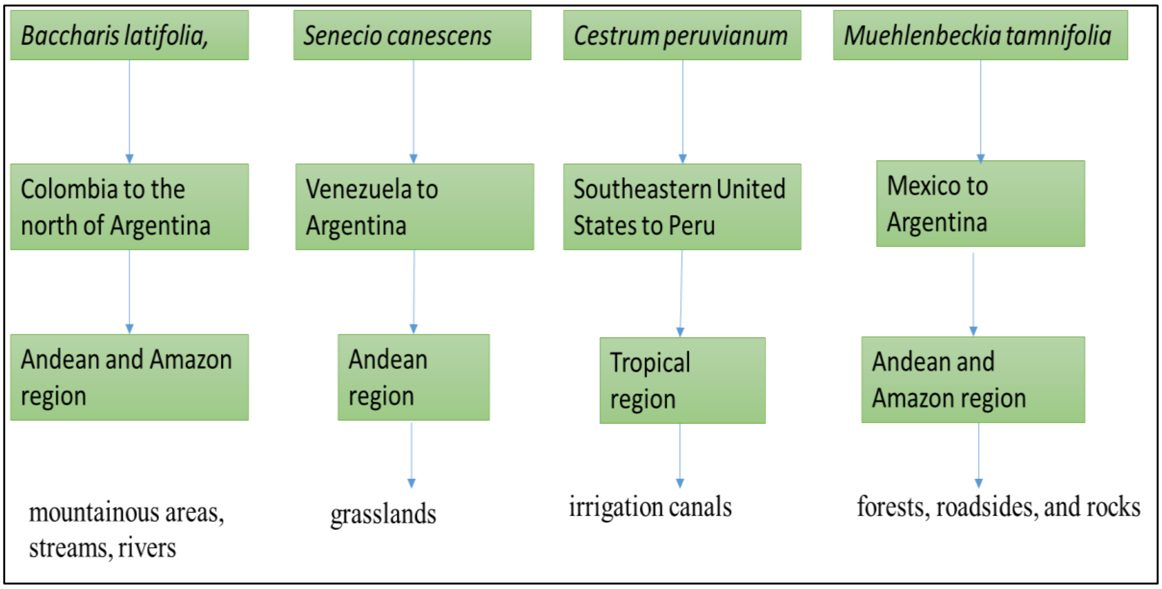

Figure 2.- Geographical distribution of *Baccharis latifolia, Senecio canescens, Cestrum peruvianum, and Muehlenbeckia tamnifolia.*

Chapter IV

4. Chemical composition of phytochemicals

Phytochemicals are diverse are classified into terpenoids and terpenes, alkaloids, phenolic, and organosulfur compounds (53).

4.1. Terpenoids or Terpenes

Terpenes are simple hydrocarbons isolate from different natural sources as plants, animals, microbes, insects, plant pathogens, and marine species (54). On the other hand, terpenoids are a modified class of terpenes with different functional groups, and oxidized methyl groups moved or removed at various positions (55). In 2017, Prakash (56), exposed that most of the terpenoids are biologically active and are used worldwide to treat many diseases. Terpenoids are classified based on the number of carbon atoms, that is to say, according to on the number C5 known as isoprene units, terpenoids classification is shown in Table 5. However, in vivo terpenes are not synthesized from isoprene units instead, all have a biosynthetic origin from acetyl-coA or its intermediates.

Table 5.- Classification, examples and activity of terpenoids.

Number of carbón	Class	Examples	Activity	Ref
C5	Hemiterpenes	Prenol, tiglic acid, angelic acid, and isovaleric acid.	-----	(57–59)
C10	Monoterpenes	α-terpinene, γ-terpinene, α-pinene, p-cymene, terpinen-4-ol, α-terpineol, 1,8 cineolepentacyclic triterpenoid, thymol, citral, mentol, carvacrol, citronellol, and limonene.	Antitumoral, antibacterial, and antiviral.	(59–62)
C15	Sesquiterpenes	Abscisic acid,	Antimicrobial	(55,57,58)

		farnesol, and artemisinin.	anti-insecticidal.	
C20	Diterpenes	Gibberellic acid, cafestol, drechmerin B.	Anti-inflammatory, antimicrobial.	(60–62)
C25	Sesterpenes	Lactone, abietic acid	Anti-inflammatory, anticancer, antimicrobial, and antifungal.	(57,58,63)
C30	Triterpenes	Betulinic Acid, oleanolenic acid, ursolic acid, cucurbitacins, lanosterol, Squalene	Bactericidal, fungicidal, analgesic, spermicidal, cardiovascular, anti- allergic, anti-parasite, anti-inflammatory, anti-diabetic and anti-viral	(60–62,64)
C40	Tetraterpenoids	Lycopene β-Carotene.	------	(57,58,63)
C>40	Polyterpenoids	Rubber.	-------	(57,58,65)

Table 5 explains the classification of terpenoids, first place, hemiterpenes, or simplest terpenes, known as isoprene (59). Next, the monoterpenes consist of two linked isoprene units; they exist in essential oils. Sesquiterpenes consisting of three isoprene units and are present in the form of a lactone ring (55,66). Four isoprene units form diterpenoids. Sesterpenes consist of five isoprene units and triterpenes of six isoprene units. Also, triterpenes can have many methyl groups and can be oxidized into alcohols, aldehydes, and carboxylic acids, making them complex and differentiate them biologically. Tetraterpenes have 40-C, constitute a large group of natural dyes and possess a variety of functions. Polyterpenes are formed by more than forty carbons (57,58,60–65).

4.1.1. Biological activity

Terpenoids are used in the medical area to improve the biological activity of humans (67). Researchers explained that terpenoids significantly inhibit the development of chronic joint swelling. Research both in vitro and in vivo showed compounds triterpenoids free form intervene positively in the inflammatory, oxidative, microbial, parasitic, and viral effects, same way, contributes positively as analgesics and hepatoprotectors (58,62,64).

4.2. Alkaloids

Alkaloid is a cyclic compound with at least one nitrogen atom in a negative oxidation state (68,69)**.** Most of the alkaloid compounds are made up of carbon, oxygen, and hydrogen, and nitrogen but on the odd occurrence, different elements like phosphorus, chlorine, sulfur, and bromine. Velu et al. (70), explained that the major source of the alkaloid is flowering plants such as angiosperm, around 20% of plant species contain alkaloids. The nitrogen atom presents in the alkaloids acts as a defense driving force that protects the plant cells against bacteria, virus, or microorganism infection. As a result, they have analgesic, antispasmodic, bactericidal effects, antiseptics properties. Besides, principal examples used in pharmacology are morphine used as analgesics, berberine as antibiotics, vinblastine as anti-cancer, and atropine as anti-cholinergic (71,72).

Alkaloids are classified into three groups, first, typical alkaloids having a heterocyclic ring with a nitrogen atom and derived from amino acids; next, biological amines, which are non-heterocyclic; finally, steroidal alkaloids having a heterocyclic ring with nitrogen atom but not derived from amino acids. Table 6 explain about most widely accepted and standard mode of chemical classification of alkaloids as pyridine, tropane, quinolones, isoquinoline, indole, imidazole, purine, and steroidal (66,73).

Table 6.- Classification of Alkaloids with examples and biological properties.

Class	Examples	Biological properties	Ref.
Pyridine	Arecoline	Activation of brain function.	(74–76)
	Lobeline	Chronic and asthmatic bronchitis.	(74,75)
	Nicotine	Insecticidal, behavior-modifying effects.	(74,75,77)
Tropane	Atropine	Anti-cholinergic effects.	(74,75,77)
	Hyoscyamine	Anti-motion sickness agents, central sedative, antiemetic, amnestic, and palliative care in pain control.	(75,78,79)
	Scopolamine	Anti-motion sickness agents, central sedative, antiemetic, amnestic effects, administered to Parkinson's patients, and palliative care in pain control.	(77–79)

Quinolones	Quinine	Antimalarial, antipyretic, anti-smallpox, anti-inflammatory. antipyretic, analgesic, antimalarial, astringent.	(78,79)
	Quinidine	Heartbeat disorders, atrial fibrillation, malaria.	(77,79)
	Cinchonine	Antipyretic, analgesic, uterine contractions inducing properties, antimalarial, astringent.	(79)
	Cinchonidine	Antipyretic, analgesic, uterine contractions inducing properties, antimalarial, astringent.	(79)
Isoquinoline	Hydrastine,	Digestive, and anti-inflammatory.	(79)
	Emetine	Antiviral, anticancer, and antiparasitic.	(77) (79)
	Opium	Analgesic, antitussive, and spasmolytic.	(78) (79)
Indole	Reserpine	Antiarrhythmic, antihypertensive, antimetabolic, and antiovulatory.	(79)
	Strychnine	Muscle relaxant.	(78,79)
Imidazole	Pilocarpine	Diaphoretic and pyretic agent, and muscarinic receptor agonist.	(77,79)
Purine	Caffeine	Analgesics, anorectants and CNS stimulant.	(77,78,80)
	Theobromine	Stimulation of metabolism.	(79)
Steroidal	Solanum	Anti-oxidant, neuroprotective anti-hypercholesterolemic, analgesic, anti-inflammatory, anti-microbial, antithrombotic, antiandrogenic, and antiarrhythmic.	(81)

4.2.1. Biological activity

In 2018, Bribi (82), explained that alkaloids present antibacterial, antifungal, anti-viral, anti-oxidant, analgesics, antiseptics, sedatives properties, anti-inflammatory, antitumor activity, and anti-viral effect. Besides, palmatine, jatrorrhizine, and tetrahydropalmatine have been reported to show in vitro antimalarial activity. The best-known examples of plant-derived alkaloids used as drugs include vincristine, vinblastine, and camptothecin used as anti-cancer agents, colchicine as a gout suppressant, morphine, and codeine as an analgesic and scopolamine as a sedative.

4.3. Phenolics

Phenolics contain a hydroxyl group OH, and an aromatic hydrocarbon group is bonded to this hydroxyl group (31,83). More than 8000 phenolic compounds are based upon their structure. Phenolics is divided into two main categories flavonoids and non-flavonoids. Flavonoids are present in the leaves and fruit skin in the epidermis, mainly in organelles such as vacuoles, chloroplasts, and chromoplasts in the form of glycosides (84). The structure of these metabolites is determined as follows C6━C3━C6 (85,86), that is, chain of three carbon atoms joined to two aromatic rings joined that form an oxygen-containing heterocyclic ring. As a result, graphically, it is designated as follows: two aromatic rings (A y Band the heterocyclic ring as C. Classification of flavonoids depend on the connection between the B and C rings, the structure of the B ring, and the hydroxylation and glycosylation patterns of the three rings (85,87). Table 7 shows the classification of phenols where flavonoids can be categorized into subclasses as flavonols, flavones, flavan-3-ols, anthocyanidins, chalcones, isoflavones, coumarins, furano-coumarins, and polyphenols. On the other hand, non-flavonoids has subclasses as phenolic acids, and tannins (84).

Table 7.- Classification, examples, and activity of phenols.

Class	Sub-class	Examples	Activity	Ref.
Flavonoids	Flavonols	Kaempferol, quercitin, myricetin	Anti-inflammatory and anti-oxidant.	(31)
	Flavones	Luteolin, apigenin and tangeretin.	Induction of apoptosis.	(31)
	Flavan-3-ols	Catechin, epicatechin, epigallocatechin, and gallocatechin.	Anti-inflammatory.	(31)
	Anthocyanidins	Proanthocyanidins, gallotanins and elagitannins.	Antioxidative and antimutagenic.	(31,33)
	Chalcones	Phloretin, and arbutin.	Anticancer, anti-oxidants, antimalarial, antiulcer, anti-viral,	(31,88)

			antiprotozoal, cardiovascular.	
	Isoflavones	Daidzein, genistein.	Fungistatic, antibacterial, antiviral, and antioxidant.	(31,89)
	Coumarins	Esculetin, umbelliferone, scopoletin, and umbelliferone	Anti-microbial, anti-viral, anti-diabetic, anti-coagulant, estrogenic, dermal photosensitizing, vasodilator, molluscacidal, sedative, analgesic, hypothermic. and anti-cancer, anti-oxidant, anti-parasitic, antihelmintic, anti-proliferative, anti-convulsant, anti-inflammatory, and anti-hypertensive.	(31,90)
	Furano-coumarins	Angelicin, imperatorin, psoralen	Fungal defense.	(31)(90)
	Polyphenols	Lignins	Blocking the pathogenic growth.	(18,31,91)
Non-flavonoids	Phenolic acids	Ferulic, affeic acid gallic acid.	Antibacterial, Antitumor, anti-inflammatory, anti-oxidant, antimutagenic and anticarcinogenic.	(31)
	Tannins	Catechutannic acid, ellagic acid and chebulic acid.	Anti-inflammatory, antiseptic, and antifungal	(31)

4.3.1. Biological activity

Flavonoids have anti-viral, anti-allergic, antitumor, antimutagenic, antibacterial, antifungal, antithrombotic, and anti-inflammatory properties, anti-oxidant, a regulator of enzymes such as cyclooxygenase, lipo-oxygenase, and xanthine-oxidase, inhibitors of butyryl choline esterase and acetylcholine esterase, and inhibitors of NF-κB. The unsaturation of the c ring, the number and position of the hydroxyl groups, the state of glycolysis could improve the anti-inflammatory properties (92,93). Therefore, the bioavailability, metabolism, and biological activity of flavonoids depend on the substitution of functional groups around their nuclear structure, the total number of hydroxyl groups, configuration, and degree of polymerization.

4.4. Organosulfur compounds

In 2019, Putnik et al. (94), explain that organosulfur compounds (OSC) are characterized by a sulfur atom bonded to the cyanate group on the cyclic or non-cyclic formation. In addition, OSC is present in the form of certain essential amino acids, for exampleelements of proteins like cystine, methionine, and cysteine; tripeptide glutathione, and enzymes, coenzymes, vitamins, and hormones. Organosulfur compounds are classified as bivalent, tri-coordinated, and tetra coordinated.

4.4.1. Biological activity

Bivalent organosulfur such as cephalosporins, captopril, D-penicillamine, ranitidine, etc have pharmacological importance. Also, they have anti-inflammatory, antiaging, antiplatelet, and immunomodulatory properties (31), anti-oxidants (95), anti-microbial, anti-inflammatory properties (96), anti-viral potential (97), and anti-cancer properties (98).

4.5. Chemical composition of native plants

4.5.1. Baccharis latifolia

In 2019, Ortuño used gas chromatography coupled to mass spectrometry (CG-MS) on a sample of essential oils from Baccharis latifolia. Ortuño determined the presence of around 55 compounds, where the metabolites with the highest percentage were alpha-phelandrene, limonene, Norhalkendin, and Andro encecalinol were part of the alpha-phelandrene was the highest percentage with around 18% of total (44). In 2019, Benito and de la Cruz indicated the presence of phenolic compounds such as quercithin, trimethoxyluteolin, hispidulin, apigeline, rhamnazin, among others, with luteolin and acacetin being the main and majority. Also, there is evidence about the presence of alkaloids and terpenic and/or steroidal compounds in Baccharis latifolia. Also, there are steroidal compounds, monoterpenes such as αfelandrene, camphene; components of the essential oil such as carquejol, sabinene, ὺfelandrene, mainly limonene. Diterpenes like clerodanes, labdanosand. Sesquiterpenes such as squalene, eudesman (92,99, 100).

4.5.2. Senecio Canenses

Chuctaya et al, determined *Senecio canescens* had metabolites such as flavonoids, among which 3, 4,5-Trimethoxy-3-o-Glycosyl flavonol stand out. In addition, alkaloids, resins, and polyphenols (43,101). In the 2017, in investigation carried out in *Senecio canescen*s by Chilquillo & Cervantes (50), the result contained alkaloids, triterpenes, saponins, and flavonoids such as isoflavones and flavones or flavonols.

4.5.3. Cestrum peruvianum

In research based on the activity of the extract of the genus Cestrum, studies demonstrated the presence of flavonoid glycosides pinoresinol, nicotiflorin, rutin, sinapoyl glucose, ursolic acid, Flavanones. Flacones, Traces of essential oil, Tannins, gums, organic acids (formic and acetic), Resin, saponins. Peñaherrera et al. (102), in the research on the anti. inflammatory of methanol extracts of plants from southern Ecuador in zebrafish found that *cestrum peruvianum* presented phenolic compounds, coumarins, saponins, and terpenoids.

4.5.4. Muehlenbeckia tamnifolia

In 2020, Crucerira, after conducting research, identified in the extracts of the leaves of Muehlenbeckia tamnifolia, nine different chemical components such as lupeol acetate, coumaric acid, lupeol, β-sitosterol, trans-p-acid coumaric, linoleic acid, (+) - catechin, afzelin, quercitrin (38). Another phytochemical investigation with *Muehlenbeckia tamnifolia* extracts by nuclear magnetic resonance determined the presence of lupeol acetate, cis-p-coumaric acid, lupeol β-sitosterol, trans-p-coumaric acid, linoleic acid, catechin, afzelin, and quercitrin. Likewise, by means of gas chromatography analysis was identifying benzyl benzoate, alpha-tocopherol (103).

Chapter V

5. Inflammation process

The word inflammation derive from the Latin word "inflammare" (104), meaning to set on fire. Inflammation is a necessary protective response (105) to maintain an organism's homeostatic conditions against infectious and non-infectious agents. According to Campos & Esteban (106), in their research about inflammation in the zebrafish model explained that the factors to produce the inflammation could be infectious such as burn, frostbite, physical injury, foreign bodies, trauma, toxins, chemical irritants, damaged cells; or non-infectious such as bacteria, viruses, and other microorganisms (107,108) . The inflammation features are redness, swelling, heat, pain, and loss of function (102,109), which result from the local immune, vascular and inflammatory cells by eliminating pathogens and promoting tissue repair and recovery. In the research about anti-inflammatory Effects in Human Health by Ruheea et al.(110), in 2020, the inflammation intervenes cell surface pattern recognition receptors (PRRs); after, inflammatory pathways are activated; next, inflammatory mediators are released; and finally, inflammatory cells are recruited. Kumar explained that when acute inflammation fails is followed by the development of chronic inflammation (111). Thus, the inflammatory response is mediated by Microbial structures known as pathogen-associated molecular patterns (PAMPs) can trigger the inflammatory response through activation of (PRRs) such as Toll-like receptors (TLRs), leading to the synthesis of proinflammatory cytokines such as interleukin-1β (IL-1β), interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α) which activate downstream proinflammatory pathways (112).

5.1. Acute inflammation

In acute inflammation, cellular, molecular events, and interactions minimize injury or infection (104) and facilitate the repair, and tissue replacement (113) lasts for few days. The beginning of the process is determined by the tissue edema, as the result, of the increase in blood flow and subsequent permeability of the blood microvessels. There is the intervention of local mediators such as prostaglandin E or histamine, proteins such as IL-10 and annexin A1; specialized pro-resolving mediators (SPMs) including resolvins, lipoxins, maresins and protectins; the endogenous gases nitric oxide (NO), hydrogen sulfide (H_2S) and carbon monoxide (CO) (114); regulatory T cells, cysteinyl leukotrienes, bradykinin, chemokines, cytokines, free radicals, vasoactive amines by resident cells in the injured tissue (115,116). Major molecules involve in pro-inflammatory effects are eicosanoids, nitric oxide, NF-κB (109) and a variety of interleukins. On the other hand, macrophages, neutrophils and mast cells constitute the cellular types involve in the inflammation. Acute inflammatory response involves modification of the vasculature surrounding the site of stress or damage to increase blood flow. This alteration is then followed by activation of innate immune cells like macrophages, dendritic cells, and mast cells, and an increase in infiltration of additional innate immune cells into the affected tissue. In certain cases, the body is unable to resolve this response or is subjected to repeated stimulation resulting in chronic inflammation **(Figure 3)** (117).

5.2. Chronic inflammation

Chronic inflammation is a process when occurs a defect in the resolution of acute inflammation, is related to cardiovascular disease, diabetes, cancer, psoriasis among others (106,118). The research by Placha & Jampilek in 2021, explains that chronic inflammation is a long-term process, can be divided into chronic inflammation as a consequence of acute inflammation or chronic inflammation arising de novo. Factors causing acute inflammation, immune hypersensitivity reactions, autoimmunity, and immunocomplexes with the involvement of T-lymphocytes, neutrophils, and some cytokines (tumor necrosis factor (TNF) (119), interleukin (IL)-1, IL-15) can cause chronic inflammation (120). The process is identified by the intervention of mononuclear cells such as macrophages, lymphocytes, and plasma cells, tissue destruction by-products of the inflammatory cells (121). In fact, if this process persists with no recovery, then tissue damage and fibrosis will ensue.

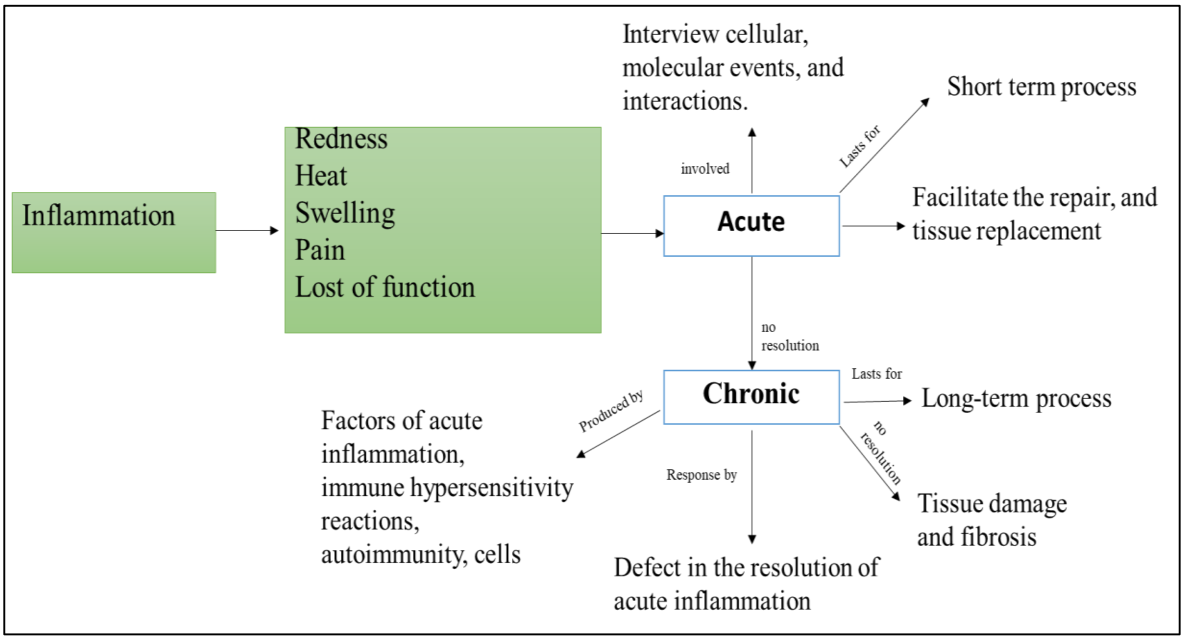

Figure 3.- Differences between the acute and chronic inflammation process.

5.3. Anti-inflammatory response

The goal of the inflammatory process is to restore homeostasis regardless of the cause. To switch off the inflammatory response is necessary for the elimination of the injurious agents that initiated it. During the inflammatory immune response, reactive oxygen species (ROS), reactive nitrogen species (RNS), and different proteases are produced that can cause tissue damage, fibrosis, cell proliferation (87). After, there is the intervention of polymorphonuclear neutrophils (PMN) that mobilized to the affected area to stop the invasion of pathogens. This mobilization is produced by chemical signals called pro-inflammatory lipid mediators (122) such as chemokines, or leukotriene B4. Next, PMNs enter into contact with endothelial adhesion receptors to cross the vasculature, finally engulf and degrade the pathogens (123). NO inhibits pro-inflammatory platelet aggregation, integrin mediated adhesion, and proinflammatory-induced gene expression. However, the overproduction of NO catalyzed by (inducible nitric oxide synthase) iNOS is cytotoxic, and high levels of NO are markers for inflammatory disorders. Macrophages, mast cells, and neutrophils are critical immune cells regulating the inflammation process, and they are an essential defensive system against pathogens. Also, macrophages produce numerous toxic chemicals such as NO and reactive oxygen species (ROS) to attack and phagocytose infected pathogens directly **(Figure 4).**

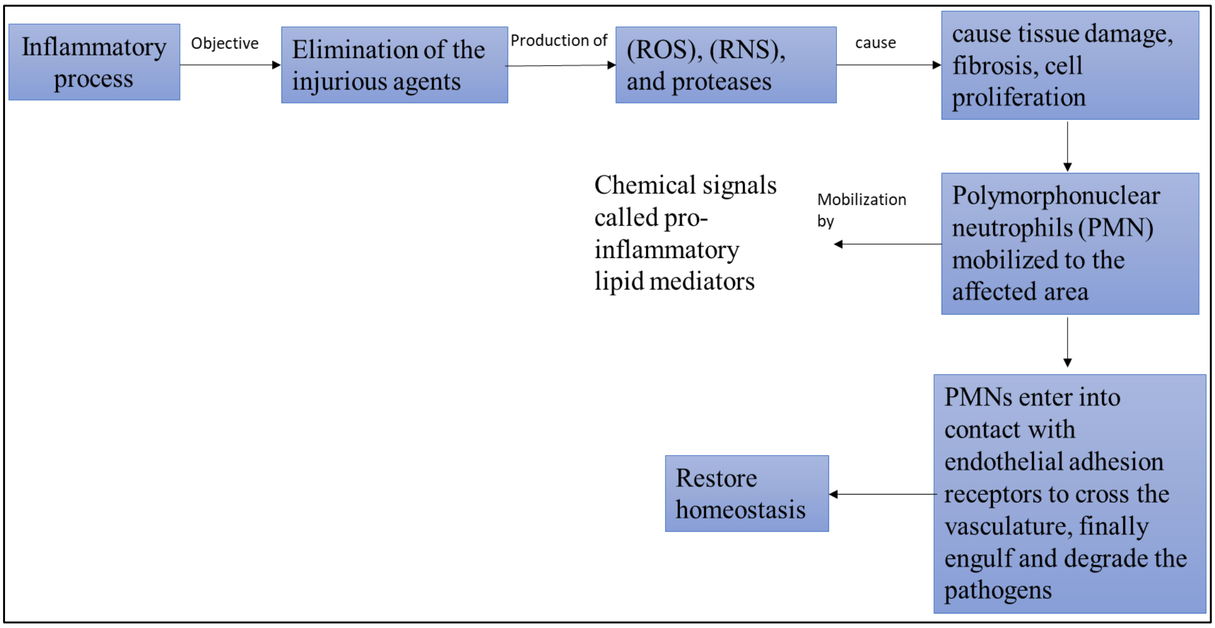

Figure 4.- Steps in the anti-inflammatory response.

5.4. Anti-inflammatory response of native plants.

5.4.1. Baccharis latifolia

There are records of investigations carried out in species of the genus Baccharis that record the presence of anti-inflammatory activity. The studies were based on ethanol extracts with flavonoids, there is evidence indicating that flavonoids can stimulate protein kinases to repress transcription factors such as NF-KB, and enzymes involved in ROS production compared to indomethacin in murine models.It was also reported that the composition of the essential oil of *Baccharis latifolia* contains limonene, which reduces inflammation and affects the production of nitric oxide, γ-interferon, and IL-4. On the other hand, the flavonoids luteolin and acacetin showed anti-inflammatory activity in mice (124). The use of this plant in an anti-inflammatory and analgesic cream was promoted in Bolivia (110). According to Enríquez et al., In their research about the content of flavonocides in *Baccharis latifolia* leaves published in 2018 indicates that in vivo anti-inflammatory activity studies with extracts of *Baccharis latifolia* demonstrated significant anti-inflammatory activity (125). Benito and de la Cruz (9), reaffirmed that phenolic compounds such as coumarins of flavonoids are responsible for the anti-inflammatory activity of *Baccharis latifolia*, and through tests, it was shown that triterpenoids also have an influence on anti-inflammatory activity **(Figure 5).**

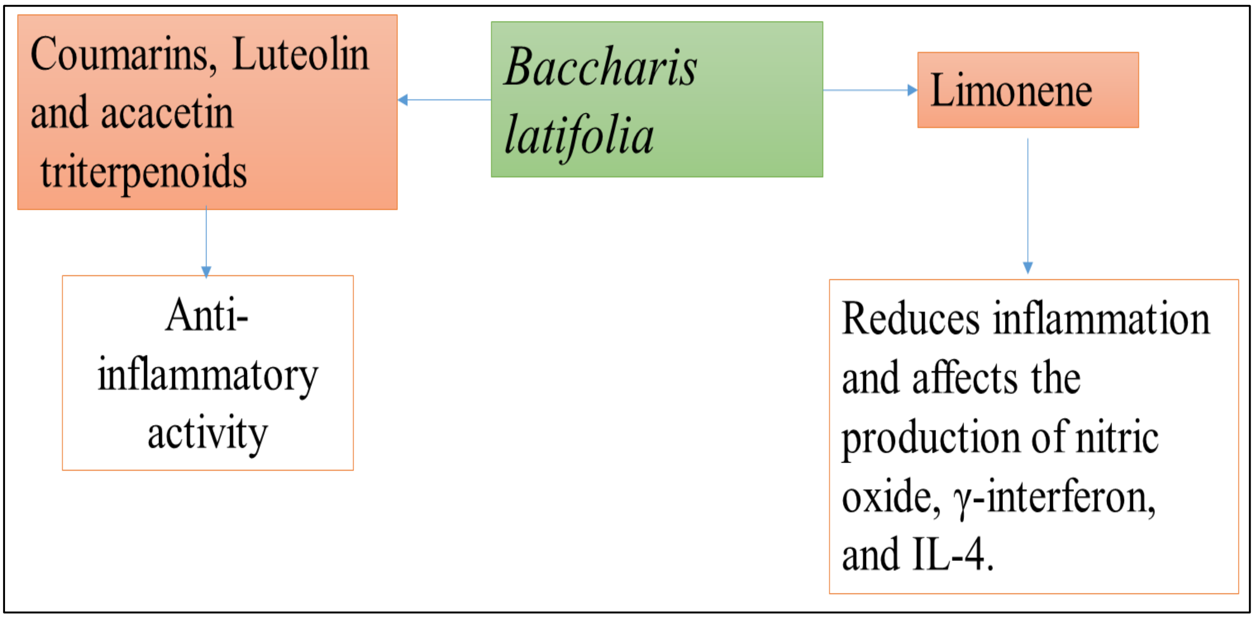

Figure 5.- Phytochemicals of *Baccharis latifolia* that interact in inflammatory process.

5.4.2. Senecio canescens

Ramirez and Benavides demonstrated anti-inflammatory properties of *Senecio canenses* through experimentation where induced plantar edema in mice with carrageenan. Carrageenan stimulates the production of prostaglandins which in turn promotes inflammatory processes. It was determined that the extract showed lower volume compared to the control group and after the fifth hour, there was a better recovery in the inflammatory process (43). Another study demonstrates the anti-inflammatory activity, ethanol extract of *Senecio canescens* was used in xylene-induced edema in the mice. The administered dose was in doses of 100 mg/kg up to 800 mg/kg of weight. It was recorded that when using 800 mg/kg it presented a greater anti-inflammatory activity, it also behaved similarly to the patterns established by Diclofenac and Dexamethasone (101). Chilquillo & Cervantes concluded that the hydroalcoholic extract of *Senecio canescens* administered orally has a greater anti-inflammatory efficacy at the dose of 500 mg/kg compared to the standards demonstrated by the administration of ibuprofen 120 mg/kg, and prednisone 1.2 mg/kg **(Figure 6)** (43,126,127).

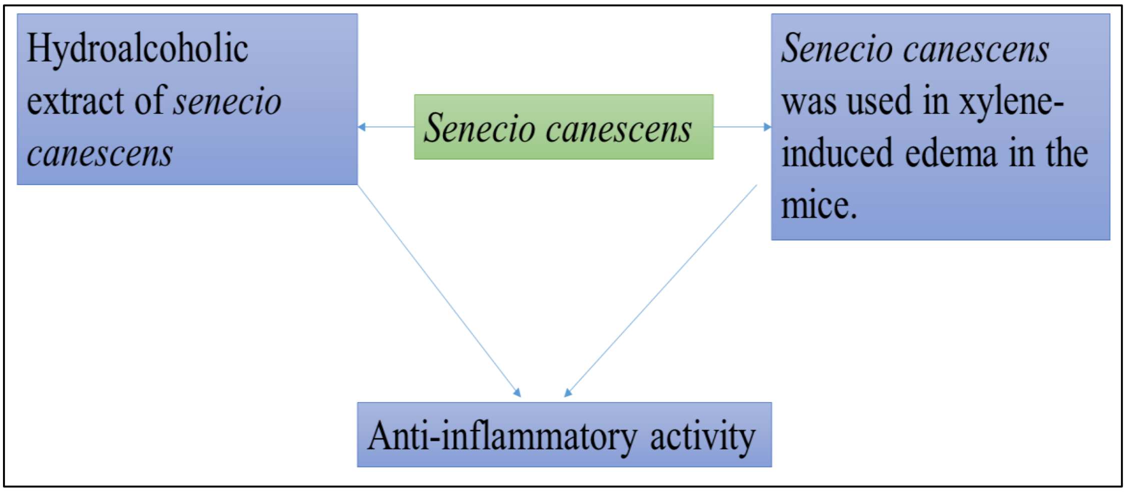

Figure 6.- Experimental investigations to demonstrate the anti-inflammatory process of *Senecio canescens.*

5.4.3. Cestrum peruvianum

Ecuadorian research on extracts of *Cestrum peruvianum* in zebrafish models concluded that anti-inflammatory activity is comparable to indomethacin and dexamethasone (128). Besides, *Cestrum peruvianum* and seven vegetable extracts compared their anti-inflammatory activity with relation indomethacin and dexamethasone; thus, the methanolic extract of *Cestrum peruvianum* was more relevant **(Figure 7)** (129).

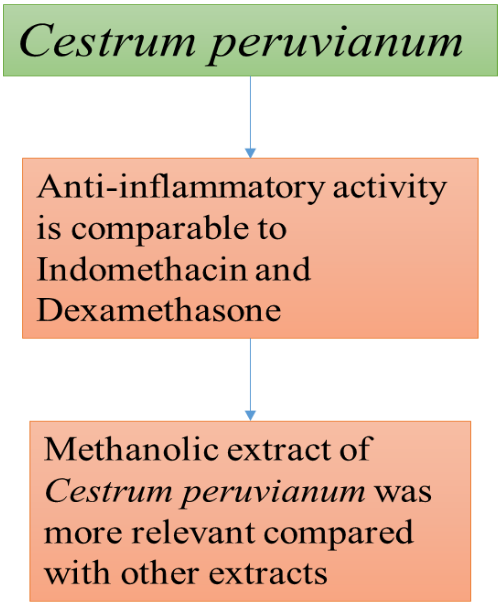

Figure 7.- Experimental investigations to demonstrate the anti-inflammatory process of *Cestrum peruvianum.*

5.4.4. Muehlenbeckia tamnifolia

Mojica et al. reported the anti-inflammatory effect of *Muehlenbeckia tamnifolia* in animal model. The research registers that the highest inhibition inflammation percentage is evidenced for the hydroalcoholic extract of *Muehlenbeckia tamnifolia* at a dose of 0.93 mg / kg, at the third hour of experimentation but two hours after a decrease in anti-inflammatory effect is observed (38). Hydroalcoholic extract from the leaves of *Muehlenbeckia tamnifolia* was also experimented with to evaluate the anti-inflammatory activity with Wistar rats, which were compared with a commercial anti-inflammatory, reporting higher values than the blank **(Figure 8)** (130).

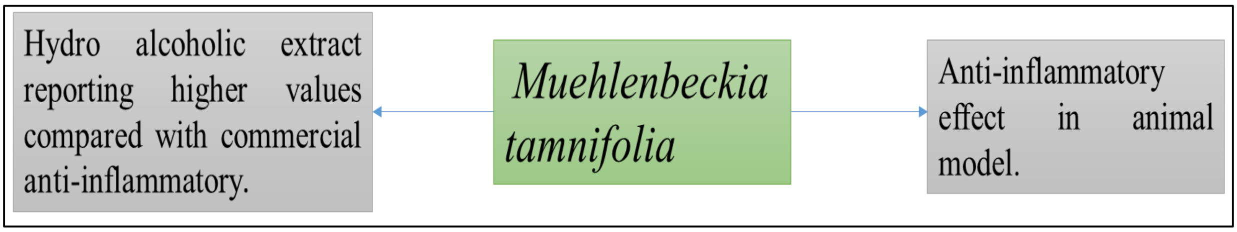

Figure 8.- Experimental investigations to demonstrate the anti-inflammatory process of *Muehlenbeckia tamnifolia.*

Chapter VI

6. Methods used for phytochemical compound extraction

There are several techniques for the extraction of metabolites present in plants. Extraction is the first step to separate metabolites from the plants, techniques to extraction are conventional and advanced. Primarily, conventional techniques use solid-liquid extraction procedures like decoction, Infusion, soxhlet extraction, maceration, and hydrodistillation (83). On the other hand, advanced technique extraction being ultrasound-assisted extraction (UAE), Microwave-assisted extraction (MAE), Supercritical fluid extraction (SFE) **(Figure 8)** (131,132). The solvent chosen for the extraction process must fulfill the following characteristics dissolve the secondary metabolites, be easy to remove, inert, nontoxic, not be easily flammable (133). Usually, the most common solvents employed are polar being water; and non-polar being petroleum ether, chloroform, diethyl ether; and semipolar as ethanol, acetone, azeotropic mixtures (134).

6.1. Conventional techniques to extraction

6.1.1. Maceration

It is a simple and economical technique based on diffusion and osmosis. In this technique, the solid to be extracted is introduced into the container and entirely covered by the solvent. To obtain the complete extraction, the container must be hermetically closed, and agitation is necessary to diffusion of compounds obtained in the liquid, on the other hand, extraction times are too long (132,135).

6.1.2. Decoction

The decoction is a method to extract the active ingredients or aromas from the parts of plants. In this technique, there is contacting the plant sample with the solvent at boiling temperature but it is not suitable for thermolabile compounds (136,137).

6.1.3. Percolation

Percolation is a method when solvent passing through the sample in one direction, reaching increasing concentrations until the secondary metabolites extraction. This type of extraction is carried out in devices called percolators. Naviglio et al. (132), mention that the wetting of the sample should be considered because it facilitates the passage of the solvent and increases the contact between the sample and solvent, and does not allow the formation of false pathways, which could impair the efficiency of the extraction. The high consumption of the solvent is considered the main disadvantage of percolation (138).

6.1.4. Soxhlet extraction

Soxhlet method is based on diffusion and osmosis principles and is the most used method for solid-liquid extraction in natural product chemistry (132). The method consists of heating a solution up to boiling, and after condensed, send back to the original flask. Ngana et al. explain that the Soxhlet method uses system it is sensitive to heat (134). This method uses a long operation time of hours or days and large solvent volumes involved, on the other hand, does not require filtration after extraction (139,140).

6.1.5. Hydro-distillation

Hydro-distillation is a traditional method for extracting plant metabolites that do not use organic solvents to remove essential oils. Heating of combination of vegetable samples and water or another solvent produce Essential oils evaporation, next, in a condenser the vapors are liquefying. There are three types of hydrodistillation: water immersion, direct vapor injection, and water immersion and vapor injection (141,142).

6.2. Alternative techniques to extraction

6.2.1. Microwave-Assisted Extraction (MAE)

MAE is a process characterized by rapid and efficient extraction through the intervention of microwaves with frequencies range from approximately 300 MHz to 1000 GHz to speed the extraction of the metabolite is necessary heat the sample and solvent, according to Naboulsi et al. in their investigation about their extraction methods and use in agriculture for controlling crop stresses and improving productivity (131). In fact, microwaves have the properties of penetrating biomaterials and interfering with polar molecules such as water present in biomaterials and then generate heat (143,144).

6.2.2. Ultrasonic Assisted Extraction (UAE)

UAE method uses ultrasound radiation that is mechanical wave energy that travels through all three states of matter (83). In fact, UAE is based on the principle of acoustic cavitation, capable of damaging the plant matrix's cell walls to favoring the release of bioactive compounds and trigger mass-transfer of phytochemicals (145). UAE requires a moderate investment of solvent and energy, easy to handle, safe, economic, and reproducible due to the fact that this technology allows its development under conditions of atmospheric pressure and at an ambient temperature (146).

6.2.3. Supercritical fluid extraction (SFE)

SFE method it is based on use a solvent called supercritical fluid (SF), generally carbon dioxide because has properties of both gases and liquids, for extraction of samples. (147,148), according to Naviglio et al. explained that Extraction can be improved by using pressure on the solubility of the desired compounds (132) . Also, carbon dioxide is non-flammable and "green", thus it has no significant impact on the environment (149,150).

6.3. Methods to isolation and purification of phytochemicals

To isolation and purification of the bioactive compounds that having different polarities is common using column chromatographic techniques. Column chromatography is a simple technique for sample clean-up and isolation of a target compound from plant crude extract (151). There are variations such as High-Pressure Liquid Chromatography (HPLC), Liquid chromatography (LC), Gas-liquid chromatography (GLC), thin-layer chromatography (TLC) (152). To identify the purified compounds, the spectroscopic techniques is used and have types like UV-visible, Infrared (IR), Nuclear Magnetic Resonance (NMR) **(Figure 8)** (153).

6.3.1. High Performance Liquid Chromatography (HPLC)

The HPLC method uses the principle of column chromatography which is based on the use of high pressure where the mobile phase is pumped.. The stationary phase is present at the bottom end of the column, while the other end of the column is attached with the source of the pressurized mobile phase high pressure (approximately 3000 psi). HPLC method is used to separate the individual components of the mixture and/or dissolved in the sample solution. Advantages are highly sensitive technique, rapid process and hence time-saving, on the other hand, irreversibly adsorbed components of the sample mixture cannot be detected, costly technique (154,155).

6.3.2. Liquid chromatography (LC)

LC is a method for analytical separation. Generally, the selectivity between analytes can be increased, the problem is about peaks can overlap with other analytes because there is not enough space in the LC chromatograms to separate the compounds (156,157).

6.3.3. Thin Layer Chromatography (TLC)

TLC is used to separate the dried liquid samples with a liquid solvent that acts as a mobile phase and a glass plate covered with a thin layer of alumina or silica gel that acts as a stationary phase. The separation of the components requires the confrontation between desorption by the solvent to eliminate the stationary phase and the adsorption process of the solute in the stationary phase. TLC method helps to identify the individual components, and visualize the points of separate components (156,157).

6.3.4. Gas chromatography (GC)

GC is a method for the separation of volatile compounds. It method is based on gaseosus phase flowing and the liquid phase is immobile. Then, the migration rate of the chemical species is determined by the distribution in the gas phase. The stationary phase is characterized by a liquid material with a high boiling point such as silicone grease or wax, which coats the inside of the column, or can be placed in an inert granular solid and packed into the column. Gas chromatography is used for the qualitative and quantitative analysis of compounds with low polarity because it has reproducibility, speed of resolution and high sensitivity (158).

6.4. Method to analysis of phytochemical

6.4.1. Spectrophotometry

Spectroscopic techniques is a process where light intervenes in combination with matter and probe certain characteristics of a sample to determine its consistency or structure. The basic principle of spectroscopy is to pass electromagnetic radiation through an organic molecule that absorbs some of the radiation, but not all of it. By measuring the amount of electromagnetic radiation absorption, a spectrum can be produced. Spectra are specific to certain bonds in a molecule. NMR spectroscopy is a technique versatile and analytical that can be applied to liquid and/or solid materials (155).

Scientists mainly use spectra such as ultraviolet (UV), visible, infrared (IR), radiofrequency, and electron beam to clarify the structure. For this reason, UV-visible spectroscopy can be performed for qualitative analysis and for the identification of certain classes of compounds in both pure and biological mixtures. In infrared spectroscopy, some of the frequencies will be absorbed when infrared light passes through a sample of an organic compound (157).

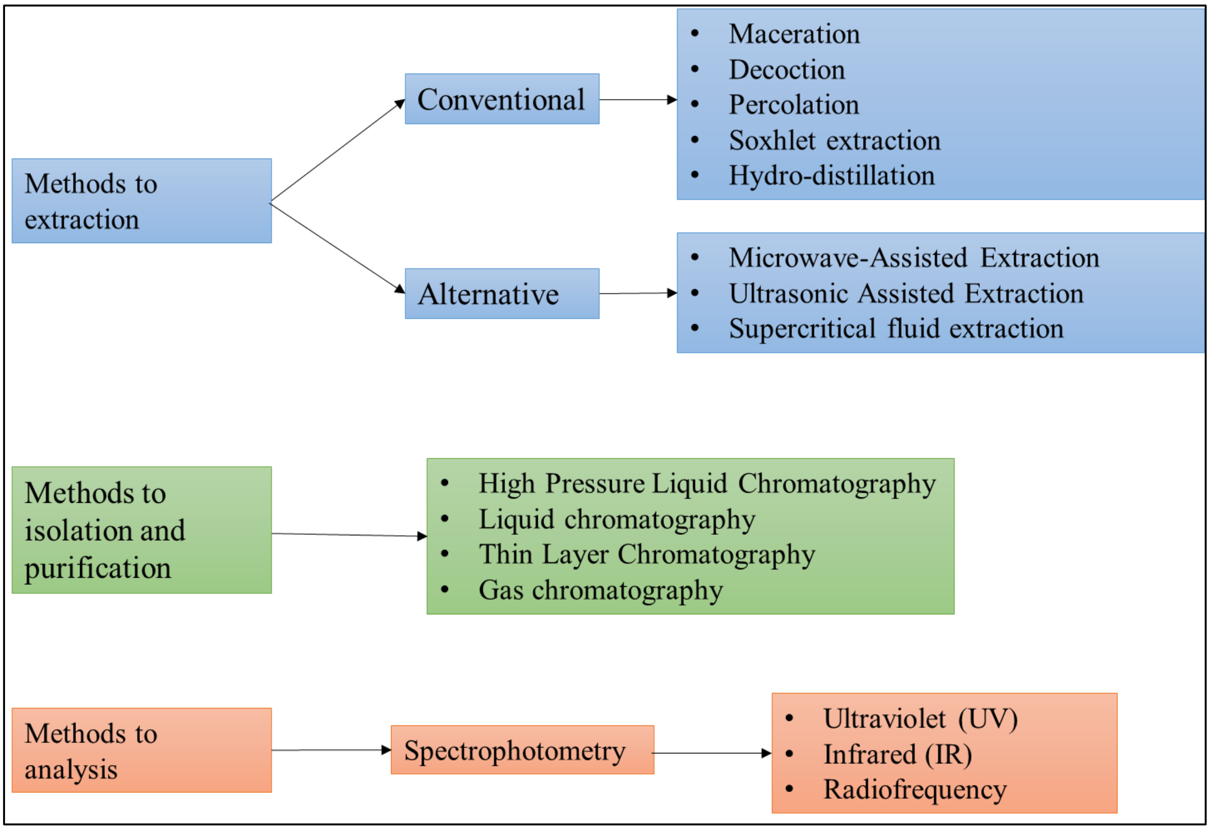

Figure 9.- Classification of extraction, isolation, and analysis methods for phytochemicals.

Chapter VII

7. Conclusion and Outlooks

Muehlenbeckia tamnifolia, Baccharis latifolia, Senecio canescens and Cestrum peruvianum species are natural resources to take relevance in traditional medicine because are tools of immediate access to counteract different symptoms or diseases. The species reviewed in the document present physical characteristics that allow them inhabit Andean areas of the American region. In addition, plant species are considered small living laboratories composed of a number of chemical elements classified by their different nature chemical. As the result, the chemical characteristics of phytochemical have influence on inflammatory, oxidative, viral, carcinogenic processes, among others. The experimental research in the plant species evaluated to determine the degree of effectiveness on antiinflammatory processes was affirmative in greater or lesser extent. It is relevant to consider that the methods used to extract phytochemicals from plant species can be classified into conventional or advanced, that depend on the nature of the extracted metabolite. Also, there are a number of techniques based on column chromatography to isolate metabolites, and spectrography is important to the analysis of these metabolites.

Although the information collected about the presence of phytochemicals with anti-inflammatory properties in the reviewed plant species is limited, future experimental research would be convenient to corroborate the reviewed information about inflammatory processes. In addition, the comparison of the amount and type of phytochemicals present in plant species located in different geographical areas would be relevant to observe the similarity or differences of the phytochemicals present.

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