

*Review*

## **Advances in the research of *Adenanthera pavonina*: From traditional use to intellectual property**

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***Adenanthera pavonina*, an Asian native leguminous, is a well known highly used plant in traditional medicine. Such broad herbal medicine applications motivated several researchers to study its chemical composition, mainly of its leaves, seeds, and barks, besides the pharmacological effects aiming to demonstrate scientific evidence of its empirical uses. Most studies have been conducted with plant derivatives, and more recent studies have focused on isolated compounds. The phytochemical screening revealed various secondary metabolites with diverse biological effects, including flavonoids, alkaloids, saponins, tannins, steroids, triterpenoids, polyphenols, anthraquinones, coumarins, glycosides and polysaccharides. Experimental studies of this plant have shown numerous pharmacological activities such as antidiarrheal, anti-inflammatory, antinociceptive, antioxidant, antimicrobial, anticancer, and others. Advances in the studies of phytochemistry and biological activity on this plant species over the last years led to the increasing interest of researchers in the protection of inventions focusing on its cosmetic, pharmaceutical and food applicability. This review summarizes the tremendous therapeutic and technological potential of *A. pavonina* that should be explored, opening new perspectives for future researches and the development of new products.**

**Key words:** Fabaceae, herbal medicine, leguminosae, plant extracts, toxicity.

### **INTRODUCTION**

Medicinal plants have traditionally been used in almost all cultures as a relevant therapeutic resource. These herbs

compounds that can be used in the synthesis and development of new drugs (Hosseinzadeh et al., 2015;

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Singh, 2015; Chen et al., 2016).

Among the plant families used in traditional medicine, Fabaceae (Leguminosae) is the second-largest family of medicinal plants (Gao et al., 2010). This family is divided into three subfamilies: Mimosoideae, Caesalpinioideae, and Papilionoideae. *Adenanthera pavonina* is an essential representative of the Mimosoideae subfamily (Souza et al., 2016). This native Asian tree has been naturalized in many parts of the world (Adedapo et al., 2009; Soares et al., 2015). The plant has a long history of traditional medical use for the treatment of many diseases, and its derivatives are used empirically for fever, vomiting, diarrhea, gout, rheumatism, furuncle, hypertension, stomach bleeding, hematuria and cancer (Pandhare et al., 2012a; Godoi et al., 2014; Kuruppu et al., 2019).

There are reports that *A. pavonina* has a wide variety of chemical compounds and biological activities (Pandhare and Sangameswaran, 2012). Phytochemical studies of different parts of this plant revealed the presence of several secondary metabolites, mainly including flavonoids, alkaloids, steroids, saponins, tannins, triterpenoids, polyphenols, anthraquinones, coumarins, glycosides, carbohydrates (Ara et al., 2010a; Dash et al., 2010; Moniruzzaman et al., 2015), and lipid derivatives (Soomro and Sherazi, 2012). Some studies have shown the predominance of some components such as linoleic acid, oleic acid, and palmitic acid in its seed's oil (Kitumbe et al., 2013).

Based on the traditional knowledge of the use of parts of this plant, several pharmacological effects of derivatives have been demonstrated, such as antinociceptive activity of leaf ethanol extract (Moniruzzaman et al., 2015), cytoprotective and anti-inflammatory activity of seed extract (Koodalingam et al., 2015); antihyperglycemic and hypolipidemic effect of the aqueous extract of seeds (Pandhare et al., 2012a); antimicrobial and antioxidant activity of bark extracts (Ara et al., 2010b); antifungal activity relates to antimicrobial peptides present in seeds (Soares et al., 2012), among others. Several studies on this species have helped to understand the toxicity and supported its traditional use.

This review is intended to provide information about botanic traditional use, phytochemistry, toxicity, biological activities, and technological prospecting of *A. pavonina* and offer insights into potential use of this plant in the development of new medicines, besides opening perspectives for future research. This work also considered articles published in the last years and patents related to *A. pavonina*. This broader approach will be valuable in assessing the scope of scientific studies and the technological potential of this species.

## METHODS

An extensive research of articles and patent applications referring to the plant species *A. pavonina*, between 2003

and June of 2019, was carried on. The keyword "*Adenanthera pavonina*" was used to search scientific articles on electronic databases including Scopus, ScienceDirect, Web of Science, PubMed and Virtual Health Library. The technological databases used were the World Intellectual Property Organization (WIPO), the European Patent Office (Espacenet), the United States Patent and Trademark Office - USPTO and National Institute of Intellectual Property (INPI). The selection of the patents was based on the following inclusion criteria: published patents containing the keyword "*Adenanthera pavonina*" in their title or abstract, without the restriction of the year of publication. The keyword was searched in Portuguese in the INPI databases, and in English in the other databases. All relevant abstracts, full-text articles, and full patent documents written in English and Portuguese were studied and included.

## Overview of scientific data

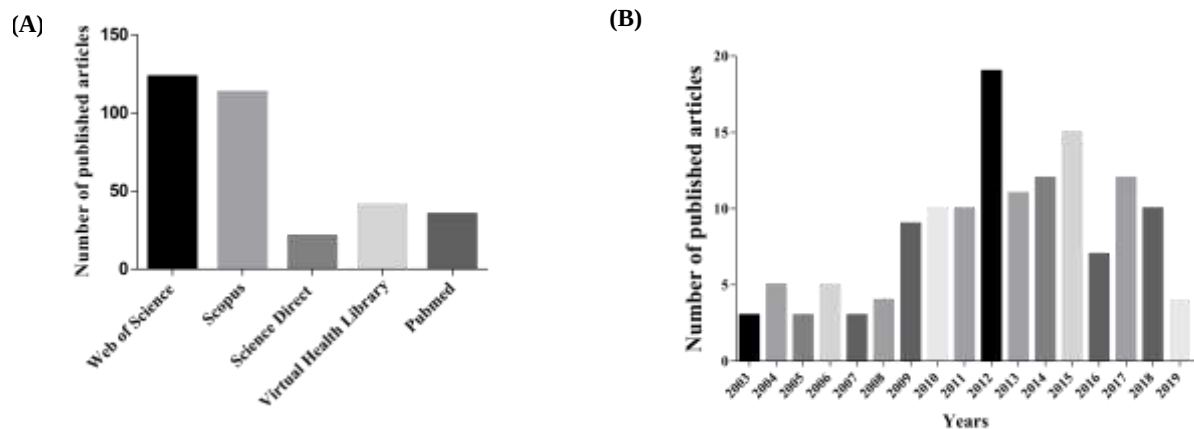
Concerning the results of the scientific productions related to *A. pavonina*, it was possible to identify, in all scientific papers database, a total of 142 articles (Figure 1A). Regarding the temporal evolution of articles, as can be seen in Figure 1B, the most significant number of publications was verified in 2012 with 13% of the total. Brazil and India were the countries with the most significant number of publications. Furthermore, based on all articles found during this time period, approximately 40% are related to the research of biological activity.

In this context, the work topics were subsequently elaborated, mainly based on the articles found in this time period, but older articles of relevance to the issue were also considered.

## BOTANICAL INFORMATION AND TRADITIONAL USES

### Botanical description

*A. pavonina* Linn. belongs to the family Fabaceae, subfamily Mimosoideae (Figure 2). This plant is a deciduous tree, usually erect, ranging in height between 18-24 m and in diameter up to 60 cm (Pandhare and Sangameswaran, 2012; Mujahid et al., 2013). It is a fast-growing tree of medium size with smooth bark of brown to greyish color, and many fissures (Rodrigues et al., 2009; Ara et al., 2010a; Dash et al., 2010; George et al., 2017). The spreading crown has few leaves. The leaves are bipinnate with 30 - 60 cm long with numerous oblong leaflets (2-5 x 0.7-2.5 cm) that are rounded at both ends and have a small point at the apex. The leaf axis is channeled on the upper surface. The flowers have corolla measured at approximately 4 mm. The fruit is a pod about 22 x 1.6 cm with quite hard seeds (George et al., 2017). The trees produce a large number of red seeds with a single seed weight on average of 0.27 g (Olajide et al., 2004; Soomro and Sherazi, 2012).



**Figure 1.** (A) Total number of articles by databases and (B) distribution of articles of all databases searched per year.



**Figure 2.** Imagens of parts of the plant *Adenanthera pavonina* L. (A) Cup of the tree (B) Seeds (C) Leaves (D) Green beans or fruits (E) Trunk (F) Inflorescence (G) Flowers.

Based on location, this plant is known as a red sandalwood tree, peacock flower fence, bead tree, coral tree, redwood, red-bread tree, Carolina tree, pigeon's eye, and dragon's eye (Olajide et al., 2004; Ara et al., 2010a; Silva et al., 2012; Mujahid et al., 2013; Godoi et al., 2014; Moniruzzaman et al., 2015). *A. pavonina* is also called a food tree because its seeds and leaves are often consumed by people (Zeid et al., 2012; Nwafor et al., 2017).

It is a species native of tropical Asia, with the first recorded appearances in India. It is common within the tropics of the old world and endemic in Southeast China and India (Olajide et al., 2004; Adedapo et al., 2009; Zeid et al., 2012; Nwafor et al., 2017). Moreover, it is an easily adaptable tree to grow on a variety of soils in humid and seasonally humid tropical climates (Olajide et al., 2004). It was introduced throughout the humid tropics and naturalized in Malaysia, Western and Eastern Africa and most island nations of both the Pacific and the Caribbean (Jaromin et al., 2006; Adedapo et al., 2009).

*A. pavonina* is a plant of diversified use. It is cultivated as forage, as an ornamental or urban tree and in reforestation. There are also reports of its use in perfumery and the manufacture of handicrafts. In addition to being used as food, especially the seeds for their high nutritional value, this species has received considerable attention for its use as a medicinal plant (Oni et al., 2009; Zeid et al., 2012; Godoi et al., 2014; Nwafor et al., 2017; Afolabi et al., 2018).

### Ethnomedicinal use

*A. pavonina* is a species that has been traditionally used as an herbal medicine for the treatment, prevention, and control of several diseases (Oni et al., 2009; Dash et al., 2010). According to the literature, this plant was used in ancient Indian medicine, where crushed seeds were used to treat boils and inflammations (Olajide et al., 2004). In general, the literature reports its empirical use for diabetes, lipid disorders, diarrhea, ulcers, stomach bleeding, hematuria, rheumatism, asthma, hypertension, pulmonary infections and chronic ophthalmia (Pandhare et al., 2012a; Zeid et al., 2012; Mujahid et al., 2013; Godoi et al., 2014; Moniruzzaman et al., 2015; Dissanayake et al., 2018) and cancer (Lindamulage and Soysa, 2016). Zeid et al. (2012) reported its use as a tonic. These reports of traditional use were most common in Asian countries (Wickramaratne et al., 2016; Koodalingam et al., 2015; Dholvitayakhun et al., 2012; Arshad et al., 2010).

Regarding the widespread use of specific parts of the plant, bark and/or leaves derivatives are used as anthelmintic, in colonorrhea, ulcers, pharyngoplasty, gout, rheumatism (Dash et al., 2010) and different painful conditions (Moniruzzaman et al., 2015); heartwood is beneficial in dysentery and haemorrhages (Dash et al., 2010). According to Olajide et al. (2004), redwood

powder is also used as an antiseptic paste. Seed extract is used for the treatment of boils, inflammations, blood disorders, arthritis, rheumatism, cholera, paralysis, epilepsy, convulsion, spasm, indigestion (Oni et al., 2009; Mujahid et al., 2013), gout, burning sensation, hyperdipsia, vomiting, fever and giddiness (Dash et al., 2010). Seed powder is used as a poultice to induce abscess suppuration (Nwafor et al., 2017).

### Phytochemical profile

There has been a growing interest in products derived from higher plants around the world. Besides being used in modern therapies, these plant derivatives are relevant for the synthesis of more complex molecules. *A. pavonina* is a plant that presents a complex and chemically varied group of compounds. Preliminary phytochemical studies on this plant revealed the presence of various secondary metabolites including mainly alkaloids, flavonoids, glycosides, carbohydrates, saponins, steroids, tannins, terpenoids and proteins (Olajide et al., 2004; Adedapo et al., 2009; Arshad et al., 2010; Dash et al., 2010; Mujahid et al., 2015).

### Phytochemical analysis of leaves

Phytochemical screening of *A. pavonina* leaves identified the presence of alkaloids, carbohydrates, proteins, flavonoids, glycosides, saponins, steroids, tannins and resins (Moniruzzaman et al., 2015; Mujahid et al., 2015).

In a search for phytochemicals, a new five-membered lactone named pavonin with an exo-cyclic double bond was identified from the methanol soluble part of *A. pavonina* leaves (Ali et al., 2005).

The presence of flavonoids in leaves, seeds, and barks of *A. pavonina* has been implicated in some biological effects of this herb (Zeid et al., 2012; Adedapo et al., 2014; Mujahid et al., 2015). Three flavonoid compounds were elucidated from the methanolic extract of the seeds of this plant: 3,5,7,3',4'-pentahydroxy flavone-3'-O- $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 4)-O- $\alpha$ -L-arabinopyranosyl-1 $\rightarrow$ 3)-O- $\beta$ -D-xylopyranoside (A) along with two known compounds 2,4,7-trihydroxyisoflavone (B) and isovitexin (C) (Appendix A1) (Yadava and Vishwakarma, 2013).

In another study, ten methoxy flavonol glycosides were isolated from aqueous EtOH extract from *A. pavonina* leaves (Appendix A2). These compounds were named as quercetin 3-O- $\alpha$ -dirhamnopyranosyl-(1 $\rightarrow$ 2 $\rightarrow$ 1 $\rightarrow$ 6 $\rightarrow$ )- $\beta$ -glucopyranoside-4'-methoxy (A), kaempferol-3-O- $\alpha$ -dirhamnopyranosyl-(1 $\rightarrow$ 2 $\rightarrow$ 1 $\rightarrow$ 6 $\rightarrow$ )- $\beta$ -glucopyranoside (B), isovitexin (C), quercetin-3-O-rhamnopyranosyl(1 $\rightarrow$ 4 $\rightarrow$ )- $\beta$ -glucopyranoside (D), quercetin-3-O- $\beta$ -glucopyranoside-4'-O-rhamnopyranoside (E), kaempferol-3-O- $\alpha$ -rhamnopyranosyl(1 $\rightarrow$ 2 $\rightarrow$ )- $\beta$ -glucopyranoside (F), quercetin-3-O-rhamnopyranosyl(1 $\rightarrow$ 2 $\rightarrow$ )- $\beta$ -glucopyranoside (G), quercetin-3-O- $\beta$ -glucopyranoside (H), kaempferol (I) and

quercetin (J) (Mohammed et al., 2014).

A chemical assay was performed to identify the lipoidal content of powdered leaves of *A. pavonina*. Analysis by gas chromatography coupled mass spectrometry of the unsaponifiable fraction (USM) identified that fifty phytocompounds represented 80.1% of the total fraction, with squalene (16.38%) as the main compound followed by n-hentriacontane (14.61%), phytol (10.29%) and 2,2-diethoxy ethanamine (8.34%). Oxygenated compounds represented 27.22% of the total fraction while the fatty acids methylated fraction presented twenty-four compounds (88.49% of the total fraction), with methyl hexadecanoate (19.25%) as the main compound followed by methyl 9,12,15-octadecatrienoate (12.69%), methyl eicosanoate (10.14%), methyl-9-octadecenoate (10.06%) and methyl 9,12-octadecadienoate (9.23%). Unsaturated fatty acids represented 32.52% of the total fraction. The gas-liquid chromatography analysis of the sterol fraction (Appendix A3) revealed a mixture of stigmaterol (A) (62.28%),  $\beta$ -sitosterol (B) (29.43%), campesterol (6.75%) and cholesterol (1.54%) (Zeid et al., 2012).

Other stigmaterol glucosides, including octacosanol and dulcitol, have also been reported in the leaves of this plant (Mayuren and Ilavarasan, 2009; Moniruzzaman et al., 2015). Zeid et al. (2012) also isolated at the first time three triterpenoid compounds identified as 22-hydroxy hopan-3-one (A), 24-methylene cycloartenol (B) and betulinic acid (C) (Appendix A4).

### Phytochemical analysis of seeds

Phytochemical screening of *A. pavonina* seeds detected the presence of cardiac glycosides, tannins, saponins, alkaloids, and flavonoids, but cyanogenetic glycosides and anthraquinones were absent (Olajide et al., 2004; Adedapo et al., 2009; Adeyemi et al., 2015).

Among the various compounds isolated and identified, O-acetyethanolamine, was extracted from the seeds of this plant (Appendix A5) (Hayman and Gray, 1987; Pandhare et al., 2017).

A study carried out to evaluate the constituents of *A. pavonina* seed oil showed their rich composition of long-chain fatty acids and fatty alcohols. Thus, a total of twelve wax ester was identified, including myristic acid arachidyl ester (C34), stearic acid stearyl ester (C36), nonadecanoic acid stearyl ester (C37), arachidic acid oleoyl ester (C38), heneicosanoic acid stearyl ester (C39), arachidic acid arachidyl ester (C40), heneicosanoic acid arachidyl ester (C41), arachidic acid behenyl ester (C42), behenic acid behenyl ester (C44), heptacosanyl stearyl ester (C45), behenic acid lignoceryl ester (C46), lignoceryl acid lignoceryl ester (C48). Long-chain fatty esters have ranged between C34 and C48, with the most portion between C40 and C48. Among the long-chain wax esters, C46 was the dominant wax ester (22.2%). The essential wax esters of *A. pavonina* were produced

mainly from the fatty acids and fatty alcohols C22 to C24 (Soomro and Sherazi, 2012).

Some work has reported the presence of proteins or peptides in *A. pavonina* seeds (Soares et al., 2012; Silva et al., 2012; Sasaki et al., 2015; Souza et al., 2016). Recently, Lavudi and Seshagirirao (2018) found an amount of protein in the crude seed extract of 82.11198 mg/ml, and a different protein profile was verified by an SDS-PAGE assay.

The seed endosperm of *A. pavonina* contains a reserve polysaccharide consisting predominantly of a galactomannan, with the general molecular structure shown in Appendix A6 (Prajapati et al., 2013). These polysaccharides present in legumes endosperm are the second largest group of reserve polysaccharides in plants (Macedo et al., 2010a). The galactomannan of *A. pavonina* L. has the ratio of mannose/galactose 1.35 and contains small amounts of other monosaccharides (Macêdo et al., 2013; Santos et al., 2015). Several studies have demonstrated the importance of this biopolymer due to its properties of water solubility and thickener, presenting thus, high versatility of application in several fields (Santos et al., 2015). Many studies using this galactomannan have been exploring the development of new formulations just like edible coatings (Lima et al., 2010), emulsion (Zarnowski et al., 2004; Jaromin et al., 2006), drug delivery (Nobre et al., 2018) and association with other materials, such as hydroxyapatite (Aquino et al., 2017).

### Phytochemical analysis of barks

Phytochemical screening of *A. pavonina* barks revealed the presence of alkaloids, flavonoids, glycosides, carbohydrates, saponin, phytosterol, phenolics, tannins, terpenoids (Dash et al., 2010; Ara et al., 2010a), proteins, amino acids and acidic compounds (Arshad et al., 2010). The phytochemical analysis also showed the presence of stigmaterol glucoside in *A. pavonina* barks (Pandhare and Sangameswaran, 2012; Pandhare et al., 2017).

### Biological activities

*A. pavonina* is a medicinal plant of traditional use that presents several scientific studies related to its biological activities. Based on their different derivatives, several activities were evaluated and confirmed by *in-vitro* and *in-vivo* studies. A brief overview of the evaluated activities of the different plant derivatives can be seen in Table 1.

#### Antidiarrheal activity

Using *A. pavonina* seeds, Pandhare et al. (2017) prepared three concentrations of aqueous extract of seeds (50, 100 and 200 mg/kg, p.o.) to the antidiarrheal test in experimental animals. The reference drug used was loperamide. This study showed that the extract

**Table 1.** Pharmacological activities evaluated using different derivatives of *A. pavonina*.

| Evaluated activity | Derivative                         | Reference                                    |
|--------------------|------------------------------------|----------------------------------------------|
| Antidiarrheal      | Aqueous seeds extract              | Pandhare et al. (2017)                       |
| Antimalarial       | MeOH seeds extract                 | Adedapo et al. (2014)                        |
| Anti-inflammatory  | MeOH seeds extract                 | Olajide et al. (2004)                        |
|                    | EtOH leaves extract                | Mayuren and Ilavarasan (2009)                |
|                    | PE barks extract                   | Ara et al. (2010b)                           |
|                    | DCM barks extract                  |                                              |
|                    | EtOAc barks extract                |                                              |
|                    | MeOH barks extract                 |                                              |
|                    | MeOH leaves extract                | Jayakumari et al. (2012)                     |
|                    | Aqueous leaves extract             | Zeid et al. (2012)                           |
|                    | EtOH leaves extract                |                                              |
|                    | CHCl <sub>3</sub> leaves extract   |                                              |
|                    | EtOAc leaves extract               |                                              |
|                    | PE leaves extract                  |                                              |
| Antinociceptive    | Aqueous seeds extract              | Pandhare et al. (2012b)                      |
|                    | EtOH leaves extract                | Moniruzzaman et al. (2015)                   |
| Anticancer         | EtOH fruits extract                | Sowemimo et al. (2009)                       |
|                    | EtOH seeds extract                 | Ferreira et al. (2011)                       |
|                    | EtOH leaves extract                | Mohammeda et al. (2014)                      |
|                    | CHCl <sub>3</sub> leaves extract   | Sophy et al. (2016)                          |
|                    | EtOAc leaves extract               |                                              |
|                    | Acet leaves extract                |                                              |
|                    | MeOH leaves extract                |                                              |
|                    | EtOH leaves extract                |                                              |
|                    | Barks decoction                    | Lindamulage and Soysa (2016)                 |
| Hepatoprotective   | Seeds powder treated enzymatically | Araújo et al. (2019)                         |
| Antibacterial      | MeOH leaves extract                | Mujahid et al. (2013)                        |
|                    | Fixed oil from seeds               | Chourasia and Rao (2005)                     |
|                    | PE barks extract                   | Ara et al. (2010a) and Hussain et al. (2011) |
|                    | DCM barks extract                  |                                              |
|                    | EtOAc barks extract                |                                              |
|                    | MeOH barks extract                 |                                              |
|                    | MeOH leaves extract                | Jayakumari et al. (2012)                     |
|                    | Aqueous leaves extract             | Dholvitayakhun et al. (2012)                 |
|                    | EtOH leaves extract                |                                              |
|                    | Hexane leaves extract              |                                              |
|                    | Aqueous leaves extract             | Thippeswamy et al. (2015)                    |
|                    | Toluene leaves extract             |                                              |
|                    | CHCl <sub>3</sub> leaves extract   | Sophy et al. (2015)                          |
|                    | EtOAc leaves extract               |                                              |
|                    | EtOH leaves extract                |                                              |
|                    | CHCl <sub>3</sub> leaves extract   |                                              |
|                    | MeOH leaves extract                |                                              |
|                    | PE leaves extract                  |                                              |
|                    | Acet leaves extract                |                                              |
|                    | CHCl <sub>3</sub> barks extract    |                                              |

Table 1. Contd.

|                     |                                                     |                                               |
|---------------------|-----------------------------------------------------|-----------------------------------------------|
|                     | MeOH barks extract                                  |                                               |
|                     | PE barks extract                                    |                                               |
|                     | Acet barks extract                                  |                                               |
|                     | CHCl <sub>3</sub> seeds extract                     | Matin et al. (2015)                           |
|                     | MeOH seeds extract                                  |                                               |
|                     | PE seeds extract                                    |                                               |
|                     | Acet seeds extract                                  |                                               |
|                     | MeOH seeds extract                                  |                                               |
|                     | Hexane seeds extract                                | Adeyemi et al. (2015)                         |
|                     | Chromatographic fractions of seeds                  |                                               |
| Antifungal          | MeOH roots extract                                  |                                               |
|                     | MeOH barks extract                                  | Rodrigo et al. (2007)                         |
|                     | MeOH seeds extract                                  |                                               |
|                     | Seed peptides                                       | Sousa et al. (2012)                           |
| Anthelmintic        | EtOH barks extract                                  | Dash et al. (2010)                            |
| Antiviral           | Aqueous seeds extract                               | Chiang et al. (2003)                          |
|                     | Aqueous fruits extract                              |                                               |
|                     | Sulfated galactomannan of seeds                     | Marques et al. (2015) and Godoi et al. (2014) |
|                     | Native and sulfated galactomannan of seeds          | Godoi et al. (2015)                           |
|                     | MeOH leaves extract                                 |                                               |
|                     | MeOH roots extract                                  |                                               |
|                     | MeOH barks extract                                  | Rodrigo et al. (2007)                         |
|                     | MeOH seeds extract                                  |                                               |
|                     | PE barks extract                                    |                                               |
|                     | DCM barks extract                                   |                                               |
|                     | EtOAc barks extract                                 | Ara et al. (2010a)                            |
|                     | MeOH barks extract                                  |                                               |
| Antioxidant         | Aqueous EtOH leaves extract                         |                                               |
|                     | EtOH leaves extract                                 |                                               |
|                     | PE leaves extract                                   | Mohammeda et al. (2014)                       |
|                     | EtOAc leaves extract                                |                                               |
|                     | CHCl <sub>3</sub> leaves extract                    |                                               |
|                     | Aqueous leaves extract                              | Thippeswamy et al. (2015)                     |
|                     | Toluene leaves extract                              |                                               |
|                     | MeOH leaves extract                                 |                                               |
|                     | MeOH barks extract                                  | Partha and Rahaman (2015)                     |
|                     | Sulfated galactomannan of seeds                     | Marques et al. (2015)                         |
|                     | Aqueous leaves extract                              |                                               |
|                     | MeOH leaves extract                                 |                                               |
|                     | EtOAc leaves extract                                | Wickramaratne et al. (2016)                   |
|                     | PE leaves extract                                   |                                               |
|                     | Galactomannan of seeds                              | Melo et al. (2018)                            |
|                     | Seeds powder treated enzymatically                  | Araújo et al. (2019)                          |
| Antihypertensive    | MeOH seeds extract                                  | Adedapo et al. (2009)                         |
| Antihyperglycaemic  | Aqueous seeds extract                               | Pandhare et al. (2012a)                       |
|                     | Galactomannan enriched food                         | Vieira et al. (2018)                          |
| Antihyperlipidaemic | EtOAc and n- butanol fractions of EtOH bark extract | Das et al. (2011)                             |
|                     | Aqueous seeds extract                               | Pandhare et al. (2012a)                       |
|                     | Galactomannan enriched food                         | Vieira et al. (2018)                          |

Table 1. Contd.

|                    |                       |                                   |
|--------------------|-----------------------|-----------------------------------|
| Renal protective   | Aqueous seeds extract | Pandhare and Sangameswaran (2012) |
| Anti-emetic        | MeOH leaves extract   | Hasan et al. (2012)               |
| Anticonvulsant     | MeOH seeds extract    | Oni et al. (2009)                 |
| Central depressant | MeOH seeds extract    | Oni et al. (2009)                 |

Etanolic (EtOH); petroleum ether (PE); dichloromethane (DCM); ethyl acetate (EtOAc); metanol (MeOH); chloroform (CHCl<sub>3</sub>); acetone (Acet).

exhibited dose-dependent significant antidiarrheal potential against castor oil and magnesium sulfate-induced diarrhea. The extract also reduced the number of diarrheal feces and the total weight of feces in a dose-dependent manner. These results confirm the antidiarrheal potential of the aqueous extract of *A. pavonina* seeds, justifying its traditional use for diarrhoea.

### Antimalarial activity

Adedapo et al. (2014) studied the different concentration of the methanol seed extract of *A. pavonina* (100, 200, 400, 600 and 800 mg/kg, p.o.) in mice infected with *Plasmodium berghei*, with chloroquine as the reference drug. The percentage parasitemia decreased significantly in the treated group with the crude extract in a dose-dependent manner. The crude extract, at a dose of 800 mg/kg exerted an antimalarial effect (92.11%) higher than that of the chloroquine (88.73%).

### Anti-inflammatory activity

Several experiments, including carrageenan-induced rat paw edema, acetic-acid-induced vascular permeability in mice, carrageenan-induced pleurisy in rats, acetic-acid-induced writhing in mice, and formalin-induced paw licking in mice were conducted to test the methanol extract of the seeds of *A. pavonina* at 50, 100 and 200 mg/kg (p.o.) using indomethacin as the standard. In all doses, the extract produced statistically significant inhibition of the carrageenan-induced paw edema in the rat. After treatment with the indomethacin and seed extract (50, 100 and 200 mg/kg), there was an inhibition of the carrageenan-induced paw edema in rats of 90.2, 34.4, 47.5 and 49.2% respectively. The extract also produced statistically significant inhibition in the acetic-acid-induced vascular permeability in mice. At a dose of 200 mg/kg, the extract caused inhibition of leakage of 61%, while indomethacin produced 75.2% inhibition. In carrageenan-induced pleurisy test, only at doses 100 and 200 mg/kg, there was a statistically significant reduction in both total and differential cell counts. In acetic-acid-induced writhing, extract inhibited the writhing syndrome in a dose-dependent manner, reflecting its analgesic effect. Indomethacin and seed extract (50, 100 and 200

mg/kg) showed an inhibition of writhing in mice by 78.6, 32.1, 44.7 and 64.7% respectively. The extract also produced a statistically significant reduction in licking time in both the early and late phases of the formalin-induced paw licking in mice, in a dose-dependent manner. Thus, results generated from this study demonstrated the anti-inflammatory and analgesic potential effects of the methanolic extract obtained from *A. pavonina* seeds (Olajide et al., 2004).

Using the ethanolic extract from *A. pavonina*'s leaves, Mayuren and Ilavarasan (2009) evaluated their anti-inflammatory effects in Wistar rats at doses of 250 and 500 mg/kg in carrageenan-induced hind paw edema tests. Also, the chronic inflammation was measured using the cotton pellet-induced granuloma formation assay. The extract caused a significant reduction in paw edema from the third hour using 250 mg/kg dose and from the second hour at the 500 mg/kg dose. At both dosages, the extract caused a significant reduction in the wet and dry weights of the cotton pellets. In the sequential study, castor oil-induced diarrhea tests were performed to assess whether the mechanism of anti-inflammatory action could be related to the inhibition of prostaglandin synthesis. Indomethacin was the standard drug. The extract significantly retarded castor oil-induced diarrhoea, suggesting the involvement of prostaglandins in its mechanism. Then, both acute and chronic inflammatory models demonstrated anti-inflammatory effects of leaf extract. These data suggest a possible anti-inflammatory activity of the active constituents contained in the leaves, such as  $\beta$ -sitosterol and stigmasterol.

Another study using carrageenan-induced rat hind paw edema model evaluated the anti-inflammatory effect of the extracts of the barks of *A. pavonina* prepared with different organic solvents (petroleum ether, dichloromethane, ethyl acetate, and methanol). The extracts were administered orally at the doses of 200 and 400 mg/kg b.w., and diclofenac sodium was the reference drug. The results showed that the fractions exhibited significant anti-inflammatory effects in a dose-dependent manner. Inhibition of inflammation between different fractions showed that the methanolic extract (400 mg/kg) reduced 37.1% of paw edema at the first hour, while the dichloromethane fraction showed, in the same dose, 33.11% of inhibition after three hours of the study when compared to diclofenac sodium. This study confirms the traditional use of extracts of the bark of *A. pavonina* to

the treatment of some inflammatory processes (Ara et al., 2010b).

Zeid et al. (2012) also evaluated the acute anti-inflammatory activity of the extracts of *A. pavonina* leaves prepared with different solvents in carrageenan-induced rat hind paw edema model. The ethanolic extract was used at the doses of 50 and 100 mg/kg body weight (p.o.), while the other extracts were administered at the dose of 100 mg/kg using indomethacin as the standard. Ethanolic extract at a dose of 100 mg/kg showed a high efficacy (91.27%) followed by aqueous-ethanol extract (89.15%), chloroform extract (79.89%), ethyl acetate extract (70.10%) and petroleum ether extract (65.34%) in comparison to the indomethacin (100%). The results suggest a possible anti-inflammatory activity of active constituents contained in the leaves such as flavonoids,  $\beta$ -sitosterol, and stigmasterol. In other findings, an active anti-inflammatory principle, O-acetyethanolamine (Appendix A5), was isolated and identified of *A. pavonina* seeds (Hayman and Gray, 1987; Pandhare et al., 2017). In another study, the anti-inflammatory activity of methanolic leaves extract was assessed by formalin-induced rat paw edema model for acute inflammation (200 and 400 mg/kg body weight, p.o.) and cotton pellet granuloma model for chronic inflammation (400 mg/kg body weight, p.o.). The results showed that the extract was satisfactory in the experimental models of acute and chronic inflammation (Jayakumari et al., 2012).

Koodalingam et al. (2015) investigated the mechanism of anti-inflammatory activity of the seed extract of *A. pavonina* on lipopolysaccharide-stimulated rat peritoneal macrophages. The results showed that the pre-treatment with the seed extracts possess beneficial anti-inflammatory effects by suppressed nitric oxide production and superoxide anion generation, cell death, and nuclear fragmentation by inhibiting the  $H_2O_2$  mediated generation of oxidative damage in rat peritoneal macrophages, suggesting that the extract has a cytoprotective property against intracellular peroxide production.

### Antinociceptive activity

Pandhare et al. (2012b) evaluated the ameliorative effect of seeds of *A. pavonina* aqueous extract in attenuating neuropathic pain in streptozotocin-induced diabetic rats during twelve weeks of treatment. Diabetic rats orally received the test extract in 50, 100, or 200 mg/kg per day and pregabalin as a standard drug. Cold and hot water tail immersion test, photo Actometer, and Rotarod tests were performed. Methods for the determination of tissue superoxide anion and total calcium levels in sciatic nerve were conducted, besides histopathological evaluation of the sciatic nerve. Surprisingly, the results evidenced that extract increased tail-flick latency significantly in diabetic rats, however, did not produce any significant effect on

motor coordination, and spontaneous motor activity of the rats. The extract also reduced superoxide anion and total calcium levels in a dose-dependent manner. Besides, the extract attenuated histopathological changes in the sciatic nerve. This study suggests that *A. pavonina* extract may attenuate the development of diabetic neuropathy in diabetic rats when compared with pregabalin and be effective in preventing the progression of diabetic nephropathy.

In another study, Moniruzzaman et al. (2015) assessed the antinociceptive activity of ethanol extract of leaves of *A. pavonina* at the doses of 50, 100, and 200 mg/kg b.w. (p.o.) using different nociceptive models in mice, including thermal tests (hot plate and tail immersion), acetic acid-induced writhing, and glutamate- and formalin-induced licking protocols. Besides, the possible mechanisms of action by the involvement of opioid receptor in analgesic activity were evaluated using naloxone and cyclic guanosine monophosphate (cGMP) signalling pathway by methylene blue. This study evidenced that the tested extract caused the reduction of nociceptive responses in a dose-dependent manner. A significant increased latency time was also observed in both thermal tests and reduction of the number of abdominal constrictions induced by acetic acid in all tested doses, evidencing the inhibition of acetic acid-induced visceral nociception, and also noting a significant inhibition of the glutamate and formalin-induced nociception. Concerning the possible mechanisms of action, this study suggests that opioid receptors and cGMP pathway may contribute to the antinociceptive actions observed in the extract. These findings demonstrate the antinociceptive activity of this extract which may be associated with its chemical compounds (e.g., alkaloids, carbohydrates, proteins, flavonoids, glycosides, saponins, steroids, and tannins) and support the traditional use of this plant in the treatment of different painful conditions.

### Anticancer activity

In the literature, there are some reports on the traditional use of *A. pavonina* derivatives to the treatment of cancer (Lindamulage and Soysa, 2016). Some *in vitro* assays have shown the anticancer activity of plant derivatives.

In a preliminary study, Sowemimo et al. (2009) demonstrated the absence of cytotoxicity of ethanolic fruit extract of *A. pavonina* against the HeLa cell line.

A study conducted by Ferreira et al. (2011) evaluated the cytotoxic potential of the ethanolic extract obtained from *A. pavonina* seeds (50  $\mu$ g/mL) in cancer cell lines. After 72 h of treatment, a low inhibition of cell proliferation against human cancer cells was observed, together with, colon HCT-8 ( $30.8 \pm 5.2\%$ ), glioblastoma SF-295 ( $23.7 \pm 3.2\%$ ), melanoma MDA/MB-435 ( $4.5 \pm 2.4\%$ ), and leukemia HL-60 ( $1.2 \pm 13.2\%$ ) cells.

In another study, the ethanolic (EtOH) leaves extract of *A. pavonina* showed significant cytotoxic activity against human hepatoma HepG2 cells ( $IC_{50} = 2.50 \mu g$ ) compared to cisplatin ( $IC_{50} > 10 \mu g$ ) (Mohammed et al., 2014).

Sophy et al. (2016) evaluated the antiproliferative effect of the *A. pavonina* leaf extracts (chloroform, ethyl acetate, acetone, methanol, and ethanol) in four cancer cell lines (HCT116, NCIH460, U251, and MCF7) by sulphorhodamine B (SRB) assay with camptothecin used as a positive control. All the extracts presented better growth inhibition of breast cancer cell line (MCF 7). However, the chloroform extract showed the best growth inhibition. On the other hand, the ethanol extract showed low growth inhibition against all the cancer cell lines.

Lindamulage and Soysa (2016) observed that a decoction prepared with barks of *A. pavonina* and *Thespesia populnea* in equal proportion, exhibited antiproliferative activity and induced apoptosis in the Hep-2 cancer cells, 24 h post-treatment.

Araujo et al. (2019) evaluated the influence of antiproliferative activity against cancer cells of *A. panonina* seed powder treated enzymatically with amylase, cellulase, and protease. The enzymatic treatment of *A. pavonina* seed powder with protease and cellulase has been shown to improve antiproliferative activity in the prostate (PC-3) and kidney (786-0) tumour cell lines.

### Hepatoprotective activity

Mujahid et al. (2013) evaluated the hepatoprotective effect of methanolic extract of leaves of *A. pavonina* against isoniazid and rifampicin-induced liver damage in rats. Animals were treated with isoniazid and rifampicin for 28 days orally to induce hepatotoxicity. Subsequently, isoniazid and rifampicin treated groups received the methanolic (50%) extract at a dose of 100 or 200 mg/kg as well as silymarin orally once daily for 28 days as the reference drug. After treatment with the extract, the serum enzymatic activities of glutamic oxaloacetic transaminase, glutamate pyruvate transaminase, alkaline phosphatase, bilirubin, and lactate dehydrogenase were restored to nearly normal levels in a dose-dependent manner. There was an increase in the levels of total protein and albumin towards normal in the methanolic extract-treated group. Restoration of hepatic antioxidant function was also verified by a significant increase in the levels of glutathione, catalase and superoxide dismutase. Interestingly, the extract avoided the elevation of hepatic malondialdehyde (MDA) formation in the liver of intoxicated rats by isoniazid and rifampicin. An histological examination observed a significant reduction in tissue damage along with minimal evidence of inflammation in liver tissue of rats treated with the extract. It is suggested that the hepatoprotective activity of the methanolic extract of *A. pavonina* may be related to the

presence of flavonoids, alkaloids, glycosides, and saponins.

### Antibacterial and antifungal activities

There have been many studies on antimicrobial activity of parts of *A. pavonina* species, and one of the oldest found was the work of Chourasia and Rao (2005) that evaluated the antimicrobial activity of fixed oil from seeds. The results showed that the seed oil showed weak activity against *B. anthracis*, *S. paratyphi*, and *B. mycoides* was ineffective against other Gram positive and Gram-negative bacteria tested.

Rodrigo et al. (2007) showed evidence of antifungal activity of methanolic extracts of roots, bark, and seeds of *A. pavonina*.

Antimicrobial activity of *A. pavonina* bark extracts prepared by petroleum ether, dichloromethane, ethyl acetate, and methanol were evaluated by disc diffusion method. All extracts were tested at different concentration (100, 200 and 400  $\mu g/disc$ ) against thirteen test bacteria: five Gram-positive (*Bacillus megaterium*, *Bacillus subtilis*, *Staphylococcus aureus*, *Sarcina lutea*, *Bacillus cereus*), eight Gram-negative (*Escherichia coli*, *Pseudomonas aureus*, *Salmonella paratyphi*, *Salmonella Typhi*, *Shigella dysenteriae*, *Shigella boydii*, *Vibrio mimicus*, *Vibrio parahemolyticus*), and three fungi (*Candida albicans*, *Aspergillus niger*, *Saccharomyces cerevisiae*). The antibiotic kanamycin (30  $\mu g/disc$ ) was the positive control. The methanolic extract had better results in the highest concentration of 400  $\mu g/disc$ , with higher inhibitory activity against *S. aureus*, *S. lutea*, and *V. mimicus*. The other extracts showed the lowest inhibitory activity at the same dose level. At a dose of 100  $\mu g/disc$ , with the exception of the methanolic extract, all were insensitive to all tested microorganisms. The authors suggest that saponins, alkaloids, tannins, and flavonoids compounds could be related to the antibacterial activity of the methanolic extract (Ara et al., 2010a).

Another study using extracts from *A. pavonina* bark at the concentration of 25, 50 and 75 mg/well, there was effective inhibition of the diameter of zones against both Gram-positive (*B. subtilis* and *S. epidermidis*) as well as Gram-negative bacteria (*Enterobacter aerogenes*, *P. aeruginosa*, *Salmonella typhimurium*) by disc diffusion method. However, the ethanolic and aqueous extracts evidenced the highest activity against all the tested bacteria (Hussain et al., 2011).

A study carried out by Dholvitayakhun et al. (2012) investigated the antibacterial activity of aqueous, ethanolic, and hexane extracts of leaves of *A. pavonina* against foodborne pathogens. Initially, the efficacy of extraction methods was assessed using the disc diffusion assay against *Campylobacter jejuni*, and erythromycin discs (10  $\mu g/disc$ ) were used as a reference. After minimum inhibitory concentrations (MICs) and minimum

bactericidal concentrations (MBCs), the best extract in the disc test were evaluated against Gram-positive (*B. cereus*, *L. monocytogenes*, *S. aureus*) and Gram-negative (*C. jejuni*, *E. coli*, *S. typhimurium*) bacteria. It was observed that the extraction method influenced bacterial activity. The aqueous extract was the most efficient to extract antibacterial constituents by the polar nature of these. However, the aqueous extract had a potent inhibition against *C. jejuni* but no activity against the other bacteria. Thippeswamy et al. (2015) also observed a significant antibacterial activity of the aqueous leaves extract against *S. aureus* and *E. coli* while the toluene extract showed activity against *E. coli*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *P. aeruginosa*, *S. Typhi*, *S. aureus*, and *Streptococcus faecalis*.

Another study, in the same year, conducted by Soares et al. (2012) evaluated the antifungal activity of peptides extracted from *A. pavonina* seeds. The results of some fractions (H11 and H22) exhibited marked inhibition in the growth of *S. cerevisiae* and *C. albicans*.

Matin et al. (2015) conducted an antibacterial screening with extracts from leaves, seeds, and barks of *A. pavonina* prepared with petroleum ether, acetone, chloroform, and methanol. All extracts were tested at the concentration of 50 and 200 µg/disc, against fifteen test bacteria: six Gram-positive (*S. aureus*, *S. lutea*, *B. subtilis*, *B. megaterium*, *B. cereus* and *Streptococcus-β-haemolyticus*) and nine Gram-negative (*S. typhi*, *S. dysenteriae*, *E. coli*, *S. boydii*, *Shigella sonnei*, *P. vulgaris*, *K. pneumoniae* and *P. aeruginosa*). Ciprofloxacin was the positive control. Minimum inhibitory concentrations (MICs) of the chloroform extract of seeds and stem wood of *A. pavonina* were also evaluated against pathogenic bacteria. Chloroform fraction of the seed extract presented the highest average zone of inhibition found to be 25 mm away from *S. β-haemolyticus*. The chloroform fraction of the seed extracts also showed promising antibacterial activity against *Serratia dysenteriae* and *E. coli*. The susceptibility order of the extracts tested was seed > leaf > stem. The MIC values of the chloroform seed extract were 256 µg/mL against *B. cereus*, 128 µg/mL against *S. β-haemolyticus*, *S. dysenteriae* and 64 µg/mL against *Klebsiella sp.* While MIC values of the chloroform extract of stem wood were 16, 32, 64 and 128 µg/mL against *S. β-haemolyticus*, *B. megaterium*, *S. sonnei*, and *S. typhi*, respectively. Satisfactory results of antimicrobial activity were also found in leaf extract extracted with chloroform, ethanol and ethyl acetate. All the three extracts displayed intense activity against *S. aureus*, *K. pneumoniae*, and *B. subtilis* (Sophy et al., 2015).

Another research about the antimicrobial activity of seed was also conducted, this time with crude extracts and chromatographic fractions of *A. pavonina* (Adeyemi et al., 2015). In this study, the crude extracts (hexane and methanolic) and 15 chromatographic fractions from methanolic extract were evaluated against different strains

of *S. aureus* (PHM 001, PHM 002, 003, PHM 004, PHM 005) in different concentrations (6.25, 12.5, 25, 50 and 100 6.25 mg/mL). Gentamicin (500 µg/mL) was used as the positive control. The methanolic extract was effective only at the highest concentration against two strains (PHM 002 and PHM 004) while hexane extract was effective at concentrations of 50 and 100 mg/mL on PHM 001. Chromatographic fraction ST 10-12F produced inhibition on PHM 002 at 50 and 100 mg/mL while fraction ST-13-15F exhibited inhibition on PHM 002 at all concentrations.

In a study of the antibacterial mechanism of action, Vasavi et al. (2015) determined the quorum sensing (QS) of ethanol extract of *A. pavonina*. The extract showed anti-QS activity in *C. violaceum* CV026 biosensor bioassay and inhibition of QS-regulated violacein production in *C. violaceum* ATCC12472. The ethyl acetate fraction was tested and resulted in changes in the virulence factor production of *P. aeruginosa* PAO1. This data showed that this extract was active as an anti-QS agent.

### Anthelmintic activity

The anthelmintic activity of the ethanolic extracts from the bark of *A. pavonina* was assessed against *Pheretima posthuma* and *Ascaridia galli*. Thus, a bioassay was developed to measure the time of paralysis and time of death of the worms in concentrations of 25, 50, and 100 mg/mL of the ethanolic extract and compared to piperazine citrate as a positive control. The results demonstrated that the ethanolic extract caused paralysis and death of worms in a comparable time to piperazine citrate, especially at higher concentration of 100 mg/mL. Dash et al. (2010) believed that the phenolic compounds in the *A. pavonina* bark extracts could be responsible for the compromise of the energy generation in the parasites by uncoupling oxidative phosphorylation, which might have paralyzed and causally led to the death of both worm species.

### Antioxidant activity

In a more incipient work, Rodrigo et al. (2007) assessed the antioxidant activity of methanolic extracts of parts of the *A. pavonina* plant by the standard 1,1-diphenyl-2-picrylhydrazyl (DPPH) method. α-Tocopherol was used as the reference. It was possible to observe a significant antioxidant activity in stem bark extract and moderate activity in root extract.

The antioxidant activity of the extracts from *A. pavonina* bark prepared with different organic solvents (petroleum ether, dichloromethane, ethyl acetate, and methanol) was measured by DPPH assay. Ascorbic acid and tert-butyl-1-hydroxytoluene (BHT) were used as positive controls. The ethyl acetate and methanol extracts presented

higher radical scavenging activity ( $IC_{50}$  value  $8.72 \pm 0.11$  and  $6.44 \pm 0.04$   $\mu\text{g/mL}$ ) when compared with the standard BHT ( $IC_{50}$  value  $27.42 \pm 0.99$   $\mu\text{g/mL}$ ). The activities of these two extracts were also comparable to the ascorbic ( $IC_{50}$  value  $5.71 \pm 0.01$   $\mu\text{g/mL}$ ), whose values were very close to free radical scavenging activity. It is suggested that the antioxidant effect may be due to the presence of flavonoids and tannins in ethyl acetate and methanol extracts of bark (Ara et al., 2010a).

A study carried out by Mohammed et al. (2014) evidenced the *in vivo* antioxidant activity of the *A. pavonina* leaf extracts. The result demonstrated that the ethyl acetate (EtOAc) extract exhibited the highest free radical scavenging activity (95.78%) followed by the ethanol extract (EtOH) at 100 mg/kg b.w. (75.35%), and chloroform extract (60.57%) as compared with vitamin E (100%). Partha and Rahaman (2015) also demonstrated the antioxidant activity by DPPH of methanolic extracts of leaf and bark (200 mg/mL), with a radical scavenging activity of 32.31 and 30.23%, respectively, when compared with ascorbic acid.

In a more complex study, Thippeswamy et al. (2015) demonstrated the antioxidant activity of extracts from leaves prepared with water and toluene using DPPH radical scavenging,  $\beta$ -carotene/linoleic acid bleaching inhibition and  $H_2O_2$  assays. All tests showed the significant antioxidant activity of both extracts.

Marques et al. (2015) evaluated the antioxidant activity of sulfated galactomannan isolated from the endosperm of seeds of *A. pavonina*. The galactomannan exhibited high scavenging activity ( $IC_{50}$  value  $7.51 \pm 0.03$   $\mu\text{g/mL}$ ). The data obtained suggest that antioxidant activity could be related to the sulfation degree and probably the mechanism of action associated with the intrinsic hydrogen-donating ability of sulfate groups.

Wickramaratne et al. (2016) demonstrated the antioxidant activity by DPPH scavenging property, and the total phenolic content of different solvent extracts of *A. pavonina* leaves. The EtOAc fraction of *A. pavonina* leaves showed the highest total phenolic content ( $34.62 \pm 1.14$  mg/g extract) and the highest DPPH scavenging activity with an  $IC_{50}$  of  $249.92 \pm 3.35$   $\mu\text{g/mL}$ .

Galactomannan from *A. pavonina* has also been shown to have a significant antioxidant effect by the reduction of DPPH radicals (Melo et al., 2018).

More recently, Araujo et al. (2019) evaluated the influence of the antioxidant activity by DPPH assay of *A. panonina* seeds powder enzymatically treated with amylase, cellulase, and protease. After treatment with protease and cellulase, an increase in antioxidant activity was observed due to improvement in the extraction of phenolic compounds.

### Antihypertensive activity

Antihypertensive effects of the methanolic seed extract of

*A. pavonina* on the blood pressure of normotensive Wistar rats were assessed. Animals were treated with the seed extract at a dose of 200 mg/kg (p.o.) once daily for 28 days and propranolol (1 mg/kg) used as the positive control. On the 29th day, the mean arterial blood pressure of the animals was measured by using a Condon manometer. The mean arterial blood pressure of the groups treated with normal saline, propranolol, and seed extract were 60, 23, and 30 mmHg, respectively. Analysis of biochemical parameters showed that the total bilirubin, total protein and the globulin fraction were significantly higher in the extract treated groups compared to the control group, suggesting that the extract has a tonic effect on the kidney and liver and these organs play a central role on its metabolism. Histopathological examination showed an insignificant change in the kidney, liver, and testes. Therefore, this study evidenced the potential of the seed extract of *A. pavonina* to cause a decrease in blood pressure in normotensive rats (Adedapo et al., 2009).

### Antihyperglycemic and antihyperlipidemic activities

Das et al. (2011) examined the antihyperlipidemic activity of *A. pavonina* L. ethanolic bark extract fractions on Triton WR-1339-induced hyperlipidemia in Wistar rats. Animals were treated, once daily for one week, with petroleum-ether fraction, diethyl ether fraction, ethyl acetate fraction and n-butanol fraction of ethanolic extract at a dose of 400 mg/kg (p.o.). Other groups received 0.3% w/v carboxy methylcellulose, CMC (vehicle control group) or atorvastatin (positive control group) 1 mg/kg. On the seventh day, 200 mg/kg Triton WR 1339 was injected (i.p.), into all the groups of animals shortly after drug treatment. Total serum cholesterol and triglycerides were measured for individual animals on the seventh day previous to drug treatment and after 24 h of Triton administration. The fractions of ethanolic extract were also administrated at the same dosage in high-fat diet-induced hyperlipidemic rats. In the results, it was observed that the ethyl acetate fraction and n-butanol fraction inhibited the rise in serum cholesterol and triglyceride levels on Triton WR 1339 administration rats. The extract fractions also significantly attenuated the elevated serum total cholesterol and triglycerides in high-fat diet-induced hyperlipidemic rats. These findings may be related to the presence of triterpenoids, flavonoids, tannins, and saponins in the fractions studied. The conclusions of the study exhibited that ethyl acetate fraction and n-butanol fraction of the ethanolic extract can adequately control the blood lipid levels in dyslipidemic situations by interfering with the biosynthesis of cholesterol and utilization of lipids.

A study conducted by Pandhare et al. (2012a) investigated the antihyperglycemic and antihyperlipidemic effects of *A. pavonina* seed aqueous extract in rats.

Initially, the effect of the extract on normoglycemic rats was evaluated. Three animal groups received seed extract orally at 50, 100, and 200 mg/kg/day (b.w.), respectively, and the control group received distilled water. Blood glucose levels were checked before and at 1, 2, 3, and 4 h after treatment. The oral glucose tolerance test was also evaluated in normal rats. Again, three animal groups received seed extract orally at 50, 100, and 200 mg/kg/day (b.w.), respectively, and the control group received distilled water. After 30 min of dosing, all the animals were given glucose (2 g/kg). Blood samples were collected before (0 h) and 1, 2, 3, and 4 h after the glucose loading and blood glucose levels were measured. The results showed that the extract at all doses did not significantly modify the blood glucose of the normoglycemic rats. On the other hand, at all doses, the extract reduced the blood glucose level in the animals that received glucose significantly after 3 h of oral administration. The antihyperglycemic activity was evaluated using streptozotocin-induced diabetes in rats (55 mg/kg, b.w., i.p.). After induction of diabetes, the rats received the extract orally at doses of 50, 100, and 200 mg/kg/day (b.w.) for 30 days, and glibenclamide, used as the reference standard. Blood glucose levels and body weight were measured on 1<sup>st</sup>, 10<sup>th</sup>, 20<sup>th</sup>, and the 30<sup>th</sup> day of the study. Treatment with seed extract in streptozotocin-induced diabetic rats showed a significant reduction in plasma glucose when compared with the control group. After treatment with the glibenclamide and seed extract (50, 100 and 200 mg/kg) there was a decrease in serum glucose levels of 74.27, 69.55, 71.45, and 72.66%, respectively, when compared with the control group. At the end of the experiment, the animals were sacrificed and blood collected to estimate biochemical parameters to the evaluation of the antihyperlipidemic activity, including plasma glucose, glycated haemoglobin (HbA1c), serum triglyceride, cholesterol, low-density lipoprotein (LDL)-cholesterol, very low-density lipoproteins (VLDL) and high-density lipoprotein (HDL)-cholesterol. It was possible to observe that treatment with the seed extract showed a significant decrease in HbA1c levels when compared to the control groups. Besides, the extracts at the doses of 50, 100, and 200 mg/kg reduced the lipid profile in diabetic rats. Lipid profile of animals showed significant reduction of 13.82, 18.08, and 22.34% cholesterol, 44.21, 51.57 and 60.00% LDL-cholesterol, 11.60, 18.13 and 18.86% VLDL and 27.43, 30.08 and 31.85% triglyceride, when compared with the control group. Significant increase in HDL-cholesterol level of 54.12, 66.62, and 70.75% was observed after treatment in the same doses. Therefore, this study speculates that seed aqueous extract *A. pavonina* has the potential to treat diabetes condition and associated lipid disorders.

In another work, galactomannan from *A. pavonina* seeds was evaluated for the antidiabetic effect in mice with streptozotocin-induced diabetes. Animals were divided

into five groups: Negative control (non-diabetic animals), diabetic control (no treatment), diabetic mice treated with 1% galactomannan enriched food, diabetic mice treated with 2% galactomannan enriched food and diabetic mice treated with metformin<sup>®</sup>. Blood samples were checked at 0, 21, and 30 days of the treatment to ascertain fasting glycemia. Total cholesterol and triacylglycerol were evaluated at the end of treatment. It was observed that the feed enriched with 1 and 2% galactomannan decreased the glycemia, total cholesterol, and triacylglycerol of the animals. This work also highlights the potential of seed biopolymer as a therapeutic alternative for the control and treatment of diabetes (Vieira et al., 2018).

### **Renal protective effect**

Another study investigated the renal protective effect of the same *A. pavonina* seed aqueous extract at doses of 50, 100 and 200 mg/kg/day in streptozotocin-induced diabetic rats. Results showed that after 13 weeks of treatment, the seed extract significantly reduced proteinuria, albuminuria, lipid levels, and HbA1c deposition in diabetic rats, suggesting the potential use of the extract in the reduction in the progression of diabetic nephropathy (Pandhare and Sangameswaran, 2012).

### **Anticonvulsant and depressant activities**

Central nervous system activities of the *A. pavonina* seed methanolic extract were conducted by Oni et al. (2009). The methanolic extract was prepared with the seed powder (80%) using a soxhlet extractor. This study used three doses of extract (50, 100 and 200 mg/kg, i.p.) which consisted of two protocols, one evaluated the anticonvulsant activity, and the other evaluated the depressant activity in Swiss albino mice. In the anticonvulsant protocol, the picrotoxin, pentylenetetrazole and strychnine were used to induce convulsions in mice, and diazepam used as a reference anticonvulsant drug for comparison. The tonic hind limb extension of the animals was considered as a manifestation of seizure. The potential of the extract to prevent the seizures or delay/prolong the latency of or onset of the hind limb extensions was considered as a sign of the anticonvulsant effect. At all doses, the seed extract not only protected mice significantly and dose-dependently against picrotoxin and pentylenetetrazole-induced seizures but also delayed the onset of seizures induced by them. The most effective protection against picrotoxin and pentylenetetrazole-induced convulsions suggest that the anticonvulsant activity of the seed extracts could be related to GABAergic neurotransmission interference or in the stabilization of nerve cells membrane in the brain. In phenobarbitone-induced sleep protocol, three doses of

the extract (50, 100 and 200 mg/kg, i.p.) were tested, and chlorpromazine used as a reference sedative drug for comparison and 2% tween 80 as the negative control. After thirty minutes, all animals received phenobarbitone. The time of loss and gain of righting reflex was considered as a measure of sleep time. In all doses, the seed extracts prolonged the phenobarbitone-induced sleeping time in mice significantly and dose-dependently. It is suggested in this study that the extract interacts with the barbiturate allosteric site on the GABA receptors, boosting the action of phenobarbitone, the effect of which might induce prolonged sleeping time.

### Antiviral activity

Antiviral effect of the *A. pavonina* seed and fruits aqueous extracts were conducted by Chiang et al. (2003). The extracts were tested against adenoviruses (ADV) and herpes simplex viruses (HSV). In the *in vitro* assays, it was observed that the aqueous extracts were effective only against ADV.

Sulfated galactomannan from *A. pavonina* has also been shown to have a relevant antiviral activity against dengue virus (Marques et al., 2015). Other researches also have confirmed the antiviral activity of sulfated galactomannan from *A. pavonina* against herpes simplex virus (Godoi et al., 2015), or of native or sulfated galactomannan from *A. pavonina* against poliovirus type 1 (PV-1) (Godoi et al., 2014).

### Anti-emetic activity

Only one study about the anti-emetic activity was reported. The crude methanol extract of the leaves of *A. pavonina* was assessed for anti-emetic activity in male chicks. Emesis was induced by copper sulphate 50 mg/kg body weight (p.o.). The anti-emetic activity was ascertained by calculating the mean decrease in the number of retching in comparison with the control. The extract (150 mg/kg body weight orally) showed an anti-emetic activity of 50.17% when compared with standard chlorpromazine at the same dose (Hasan et al., 2012).

### Other activities

Because it is a medicinal plant, the focus of this research towards pharmacological activities. However, other biological activities have been conducted as can be seen below.

Silva et al. (2012) demonstrated the bioinsecticidal effect of the *A. pavonina* seed proteinase inhibitor (ApTI) for the control of *Diatraea saccharalis*. In another study, Sasaki et al. (2015) showed that the *A. pavonina* seed proteinase inhibitor (ApTI) also caused a significant effect on *Aedes aegypti* larvae exposed to a non-lethal

concentration of ApTI during short- and long-duration assays, decreasing survival, weight and proteinase activities of midgut extracts of larvae. Other research conducted with the same seed proteinase inhibitor showed that purified ApTI resulted in an inhibition of growth of *Anagasta kuehniella* (Lepidoptera: Pyralidae) (Macedo et al., 2010b). Based on this seed proteinase inhibitor (ApTI), Rodrigues et al. (2018) developed a new promisor synthetic antimicrobial peptide called Adenovin.

In another study, Ito et al. (2018) were able to prove the inhibited effect of different extracts (bark and fruit) of *A. pavonina* against tyrosinase and collagenase.

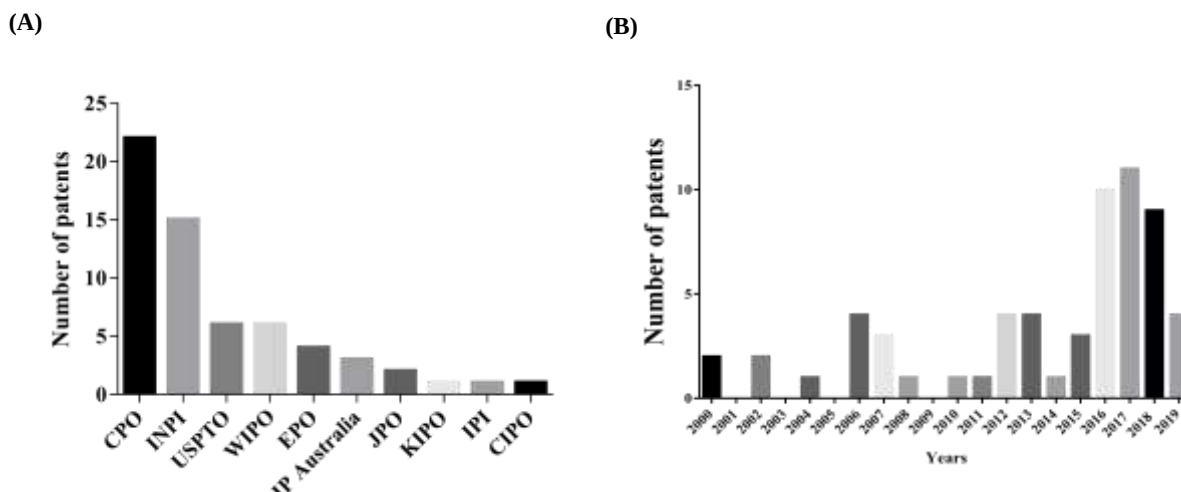
### TOXICITY STUDIES

Some studies have been conducted to evaluate the toxicity of derivatives from *A. pavonina*. Leaf extracts of this plant were screened for toxicity to brine shrimp *Artemia salina* and presented absence of cytotoxicity (Wickramaratne et al., 2016). However, the root and stem bark extracts showed cytotoxicity against *A. salina* (Rodrigo et al., 2007; Zeid et al., 2012).

Acute oral toxicity test of the ethanol extract of *A. pavonina* leaves was performed in mice. This test revealed nontoxicity up to 5000 mg/kg, demonstrating the safety of this extract (Mayuren and Ilavarasan, 2009). Another study conducted with the ethanolic extract from the leaves of *A. pavonina* revealed that the median lethal dose (LD<sub>50</sub>) of the total ethanol extract was found to be 5.8 g/kg (b.w.). This result showed that this plant derivative is considered safe (Zeid et al., 2012). As expected, Moniruzzaman et al. (2015) did not observe the toxicity of the ethanolic extract from the leaves at 2000 mg/kg. Mujahid et al. (2013) performed the acute oral toxicity study of the methanolic extract of leaves of *A. pavonina* according to the OECD 425, 2001. The results showed that the methanolic extract was safe up to a dose of 2000 mg/kg. Adedapo et al. (2014) observed that the methanol extract of *A. pavonina* exhibited an LD<sub>50</sub> bigger than 8000 mg/kg.

In another study, the brine shrimp lethality assay against extracts of the leaves of *A. pavonina* prepared with chloroform, ethyl acetate, acetone, methanol, and ethanol was conducted. The LD<sub>50</sub> values of ethanol, methanol, acetone, ethyl acetate, and chloroform were 256, 602, 681, 910 and 1387 µg, respectively (Sophy et al., 2016).

Literature reports reveal that raw seeds are toxic but can be eaten after cooking (Zeid et al., 2012). Based on this information, some studies with the seed extracts were performed. A study performed with an emulsion containing seed oil of *A. pavonina* decreased in hemolytic activity and protective effect against sheep erythrocytes (Jaromin et al., 2006). Acute intraperitoneal toxicity of the methanolic seed extract of *A. pavonina* in mice demonstrated an LD<sub>50</sub> value of 1.36 g/kg. However, the



**Figure 3.** (A) Total number of patent documents by patent offices and (B) distribution of patent applications of all databases searched per year.

extract generated a dose-dependent reduction of motor activity, with 800, 1600, and 3200 mg/kg (b.w.) doses (Olajide et al., 2004). On the other hand, the LD<sub>50</sub> of the seed aqueous extract of *A. pavonina* was higher than 2,000 mg/kg (b.w.) when administered orally (Pandhare et al., 2012a). Adedapo et al. (2009) observed an absence of toxicity in the kidney, liver, and testes of rats treated with a methanolic extract of the seeds of *A. pavonina* (200 mg/kg, p.o.). An interesting study evaluated the toxic potential of the purified trypsin from seeds of *A. pavonina* using *A. salina* lethality test. The results showed that a concentration of 0.16 mg/mL was enough to kill 100% of *A. salina* after 72 h (Souza et al., 2016).

In a recent study, Melo et al. (2018) proved the absence of toxicity of the seed biopolymer by the *A. salina* test. Therefore, it can be concluded that the *A. pavonina* derivatives were more often non-toxic. These results helped to conduct the pharmacological tests with more safety.

## TECHNOLOGICAL PROSPECTING

The technological databases used were the INPI (National Institute of Industrial Property, Brazil), USPTO (United States Patent and Trademark Office), WIPO (World Intellectual Property Organization), EPO (European Patent Office - Espacenet), and The Patent Lens (the patent data, Cambia and Queensland University of Technology). The selection of the patents was based on the following inclusion criteria: published patents containing the keyword "*Adenantha pavonina*" in their title, abstract or body without the restriction of the year of publication. The keyword was searched in English. All patent documents written in English were

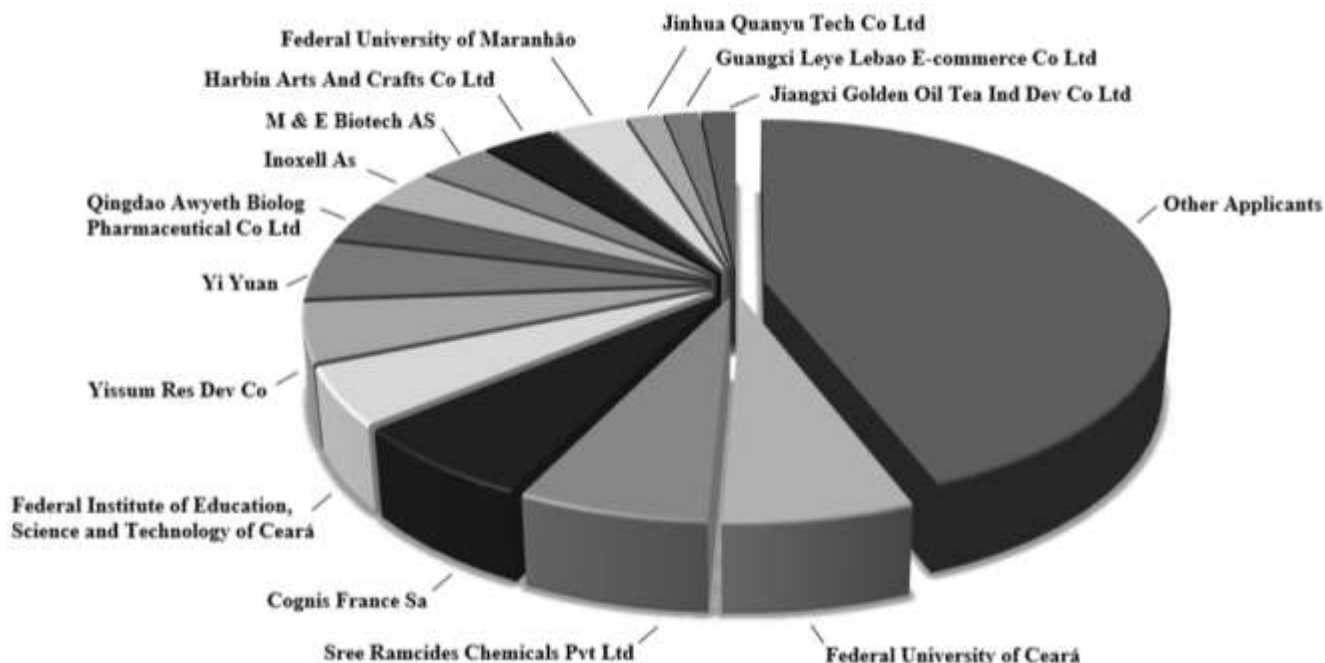
evaluated and included.

Despite the large number of publications with *A. pavonina*, this work showed a discrete number of patent applications related to this species. From the search of the patent databases, it was possible to identify a total of 61 patent documents, with 17 granted patents and 44 patent applications. Besides, the Chinese Patent Office (CPO) obtained the highest number of patent filings involving *A. pavonina* (Figure 3A). Several patent applications for the same invention were carried out in independent offices. It was possible to observe that the same inventions were applied in several countries. Therefore, the decision of a company or institution to patent in a specific country signals a purpose to enter into a local market, and the intention to patent in several countries signals to expand this market (Dechezleprêtre et al., 2017).

It is believed that the advances in researches on this plant species and the increase in the general number of publications over the last years led to the growing interest of researchers in protecting inventions.

Several countries have filed patent applications, highlighting China, Brazil and the United States. Brazil leads the number of published articles. On the contrary, China presents more patent applications than scientific publications (Appendix B).

The analysis of patent evolution in all databases showed that the first registration involving *A. pavonina* occurred in 2000. The patent entitled 'Chemistry metallurgy/biochemistry beer spirits wine vinegar microbiology enzymology mutation or genetic engineering/microorganisms or enzymes compositions thereof/modified by introduction of foreign genetic material' (WO 2000/005406 A1 and AU 1999/048985 A) was the first document found when comparing all databases.



**Figure 4.** Representation of all applicants of patents.

As can be seen in Figure 3B, in 2017, the most significant number of patent applications was carried out. It is believed that with increased investment in research on the plant, researchers have awakened the interest of protecting their inventions.

Figure 4 shows the main entities applying for patents with companies, academic institutions, and independent researchers among the main assignees.

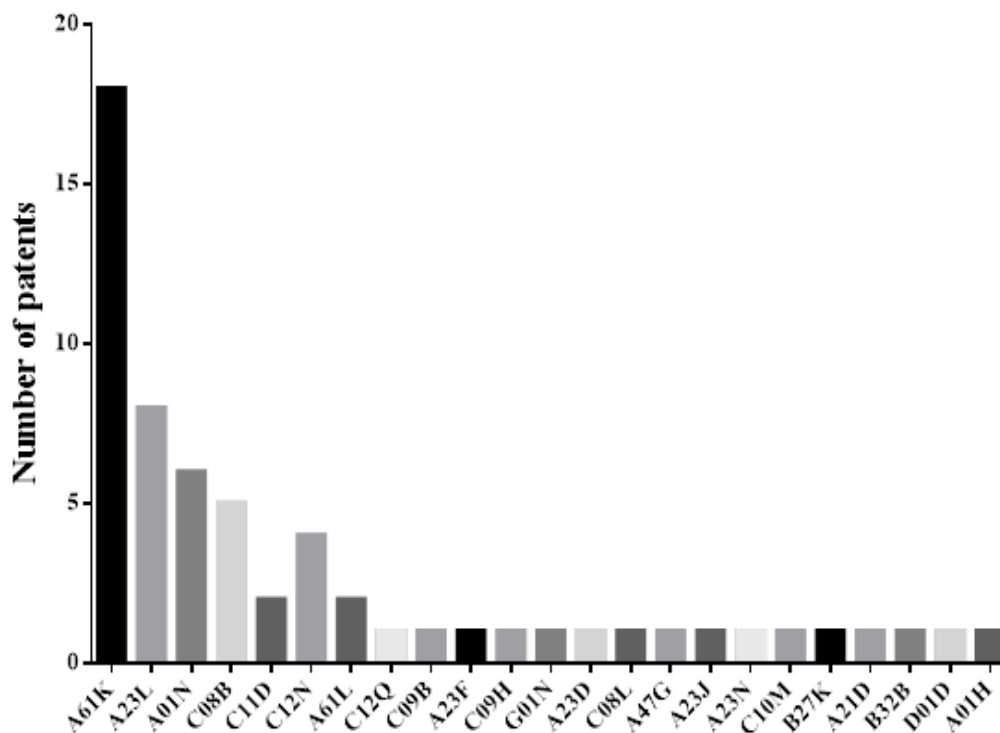
The patent documents were analyzed according to the International Patent Classification (IPC) (Figure 5), and it was observed that Section A, regarding the human needs, had the largest number of applications, followed by Section C (chemical and metallurgical) and B (processing and transportation). It was possible to observe, assessing the contents of the patents, that several of them involved the use of the biopolymer of *A. pavonina* seeds. These biopolymers are hydrocolloids which form highly viscous and stable aqueous solutions, applied as excellent reinforcers and stabilizers for emulsions, thickeners, flocculants, emulsifiers, and gellants. Due to the excellent properties of this biopolymer, it becomes an attraction for use in the textile, pharmaceutical, biomedicine, cosmetics, and food industries (Cerqueria et al., 2009). Other records involve the plant extracts for soap manufacturing and the seed extracts for the preparation of dermatological formulas for the treatment of the skin and scalp as well as the preparation of foods such as sweets and beverages (Appendix B).

It is believed that a higher number of proposals of patent applications of the plant in the biomedical area is

related to the significant part of researches on its chemical and medicinal properties. However, compared with other plant species, the search for protection of this species is still superficial. Therefore, this work showed the potential of the *A. pavonina* species in the biomedical area and opens perspectives for future discoveries.

## CONCLUSION

In this review, it was possible to verify the range of knowledge related to the *A. pavonina* species. The spread of this native Asian species to other continents and its popularity as an herbal medicine aroused particular interest in studying this plant. This species has a long history of ethnomedical use with indications for various diseases such as diarrhoea, inflammations, diabetes, rheumatism, asthma, hypertension, among others. This broad application motivated many researchers to study the phytochemistry, mainly of leaves, seeds, and barks, besides the pharmacological effects aiming to demonstrate scientific evidence of these empirical uses. Experimental studies of this plant have shown numerous pharmacological activities, such as antidiarrheal, anti-inflammatory, antinociceptive, antioxidant, antimicrobial, anticancer, etc. Interestingly, the extracts did not present high toxicity in the experimental models evaluated. It was also observed that most studies are conducted with plant derivatives, and more recent studies have been concerned with isolating, characterizing, and biologically evaluating these



**Figure 5.** Distribution by International Patent Classification (IPC) of the patent documents found in the all databases.

compounds. Nevertheless, further research is necessary to identify and investigate the pharmacological mechanisms of these main active molecules. Despite the number of studies performed, few preclinical and clinical studies have been conducted to ensure efficacy and safety in traditional therapy. In this context, considering the risk-benefit of the use of medicinal plants, more research needs to be carried out to evaluate the potential toxicity after sub-chronic, and chronic administration of this species. Therefore, this work has shown the potential of the *A. pavonina* species in the human health area and reveals outlooks for future studies. Thus, it is believed that further research with this species will lead to the discovery of prototype molecules that can be used in the development of new herbal medicines, and those new species-related patents will be filed in the near future.

## CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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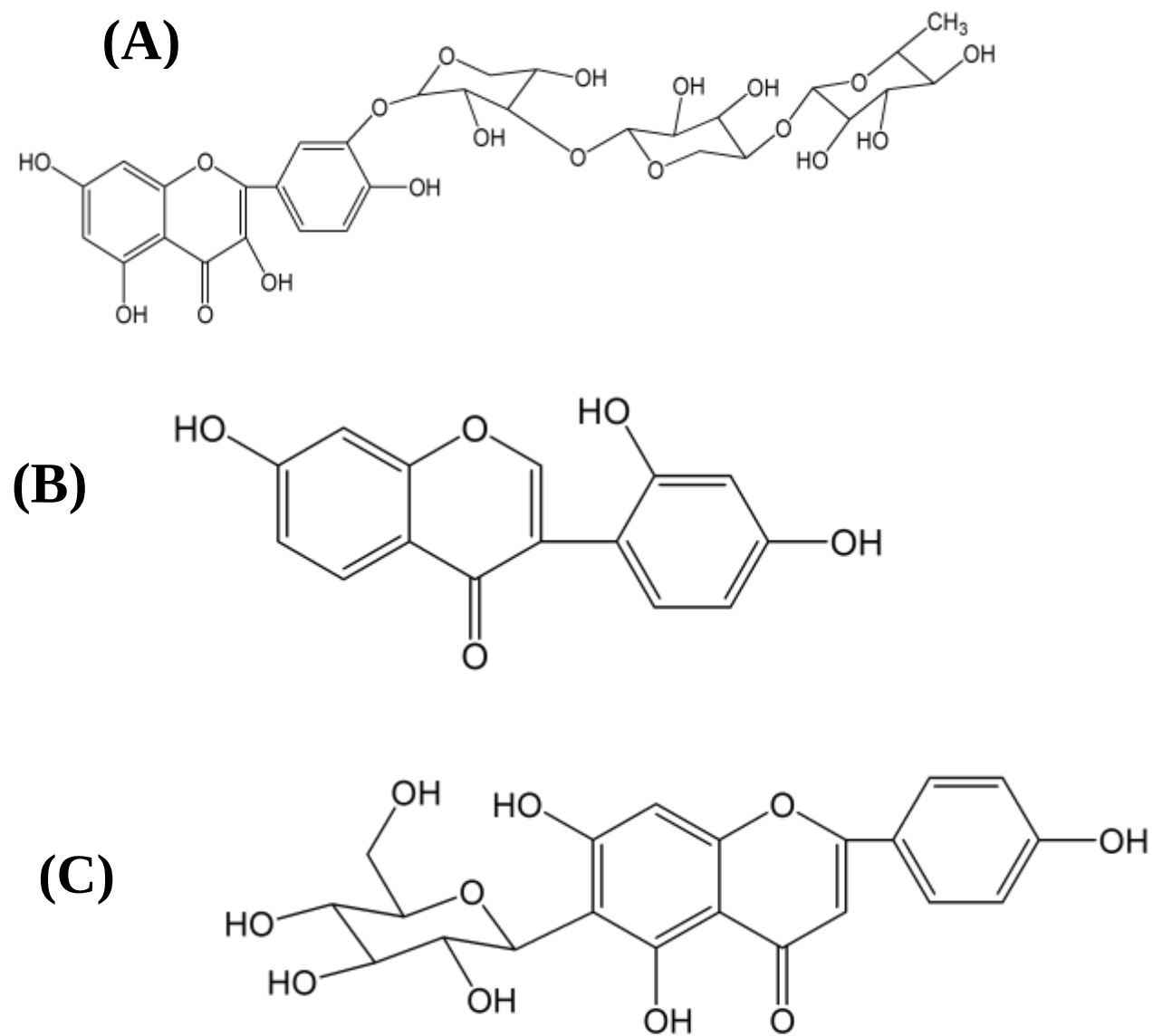
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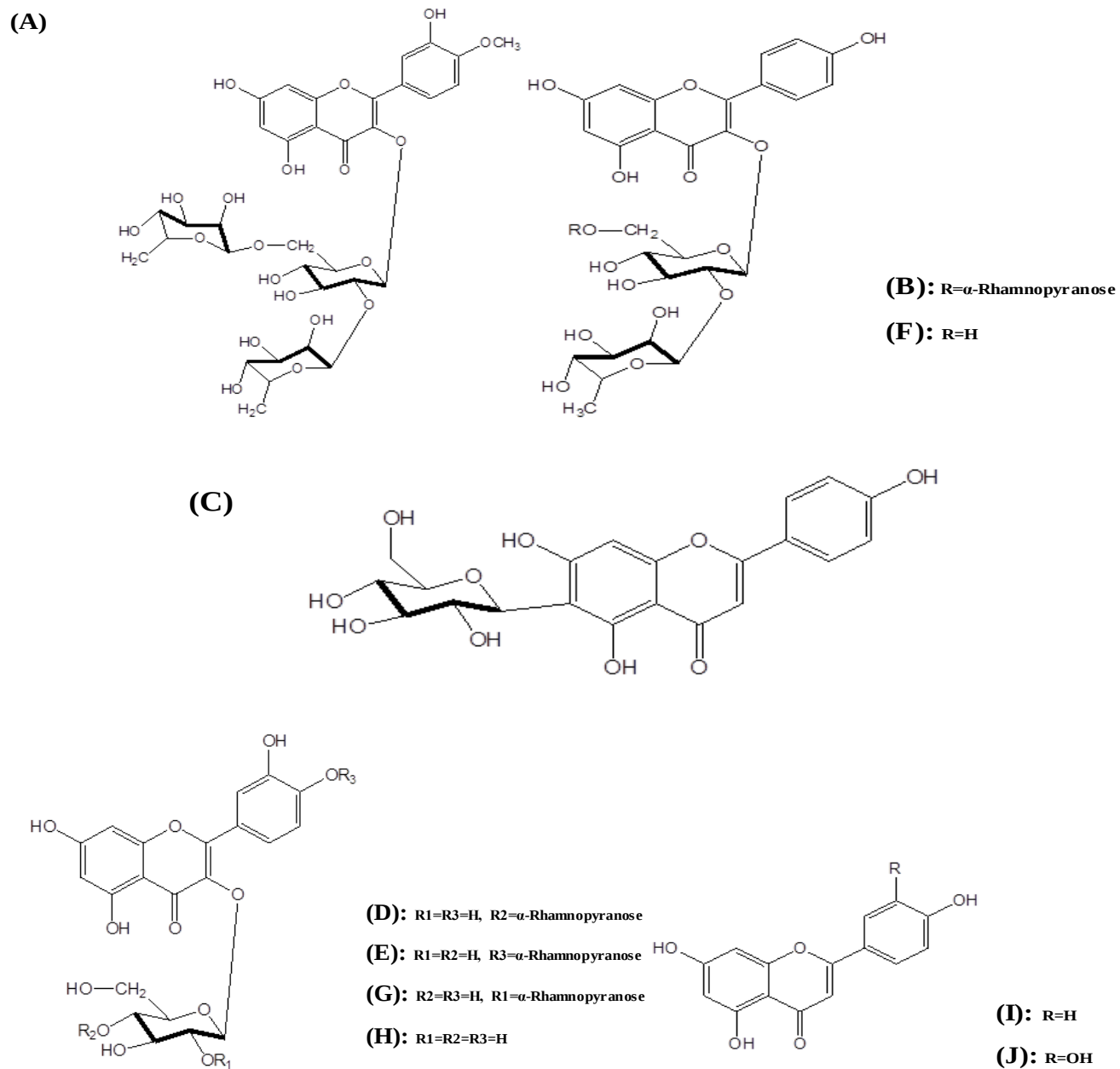
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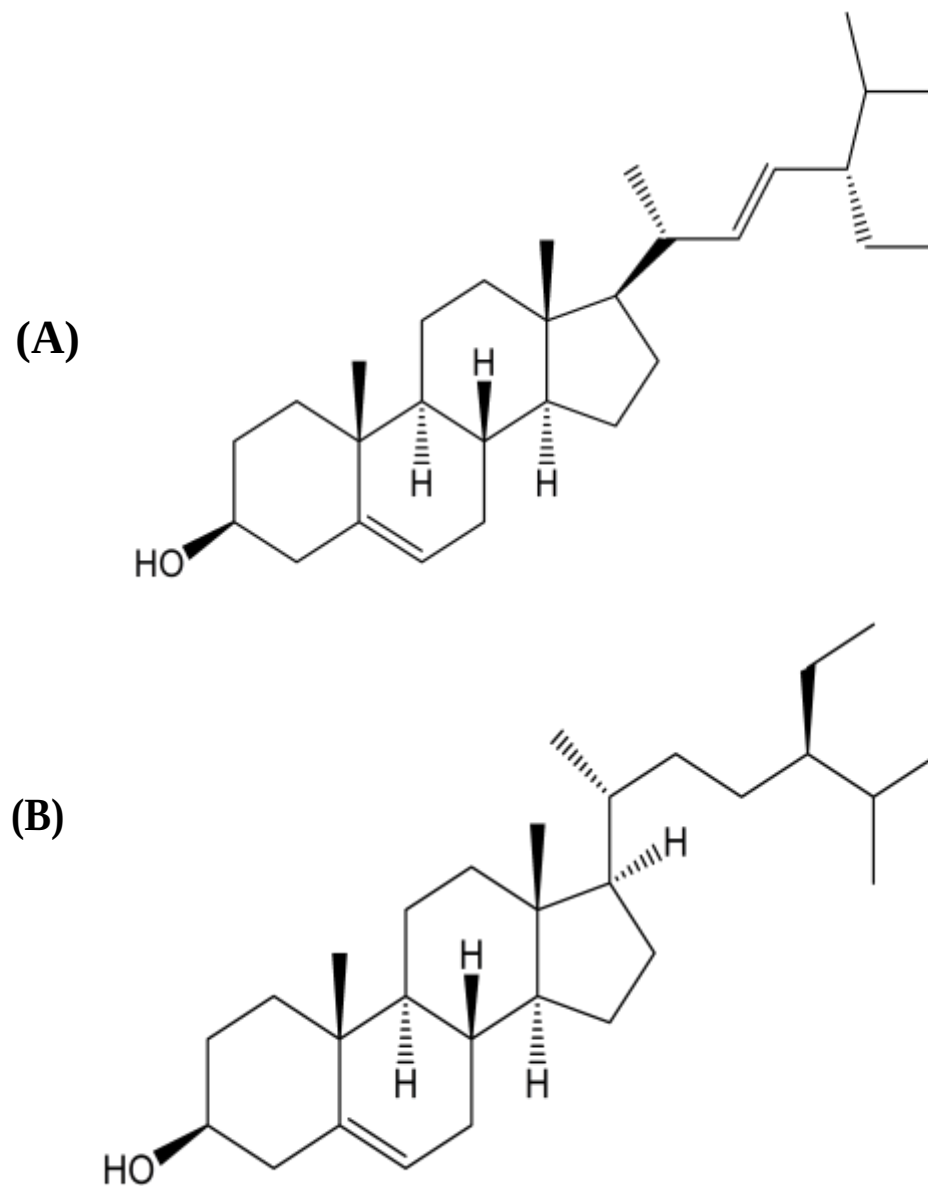
## APPENDIX



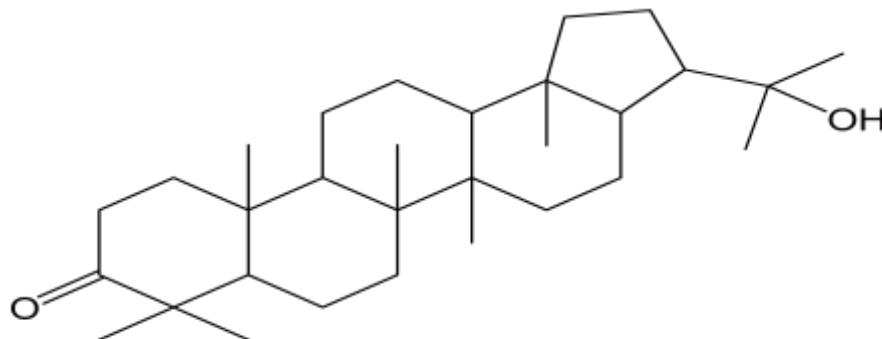
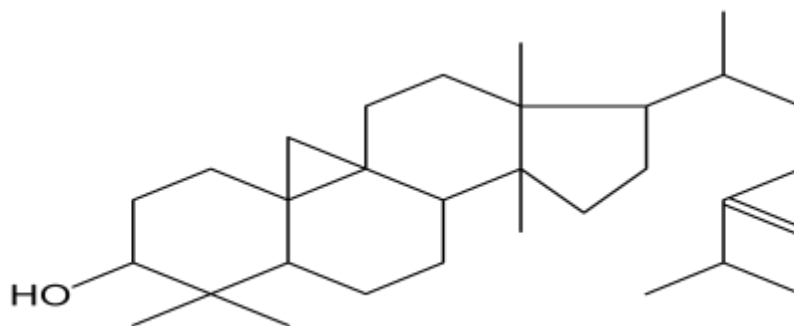
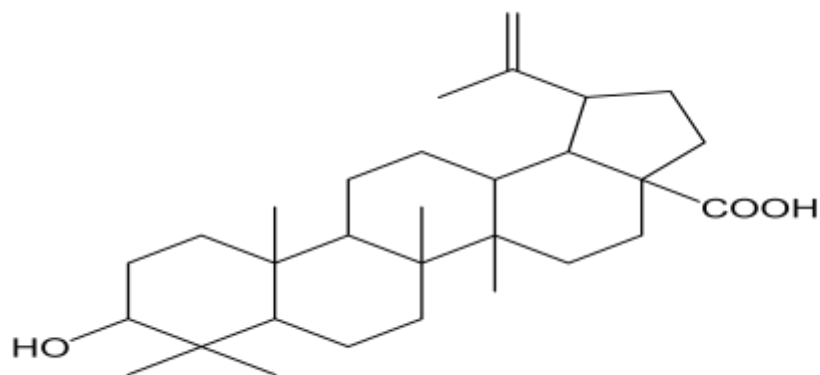
Scheme A1. Chemical structures of compounds A-C.

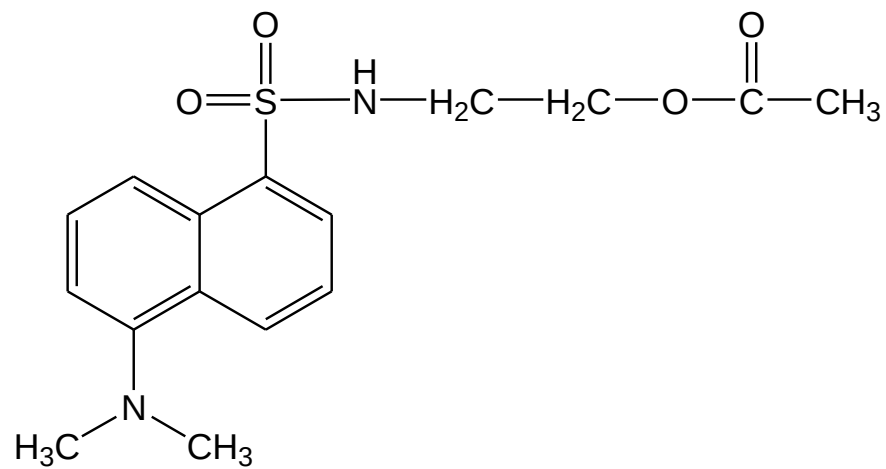


**Scheme A2.** Chemical structures of compounds A-J.

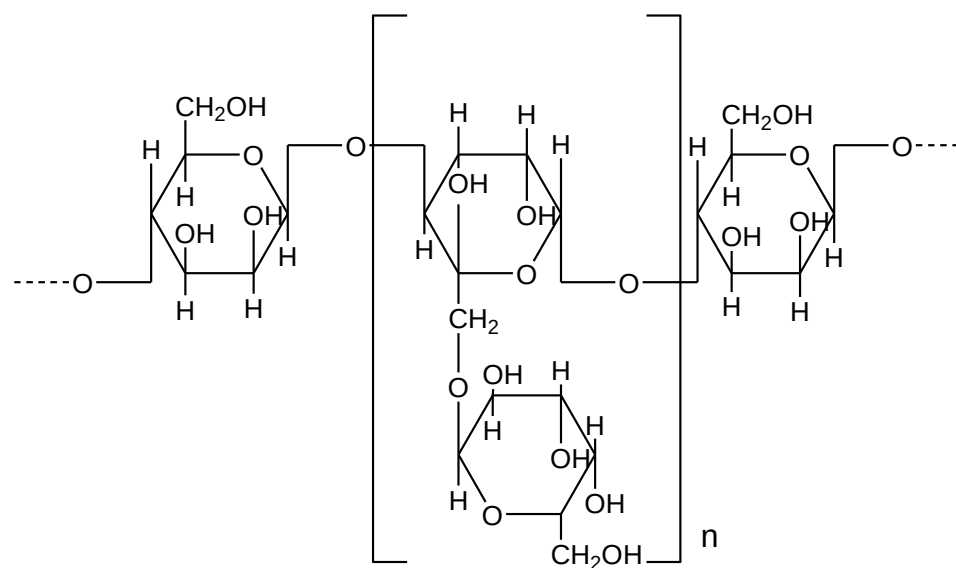


**Scheme A3.** Chemical structures of compounds A-B.  
Source: Sriraman et al. (2015).

**(A)****(B)****(C)****Scheme A4.** Chemical structures of compounds A-C.



**Scheme A5.** Chemical structures of compound O-acetyethanolamine.  
Source: Hayman and Gray (1987).



**Scheme A6.** Chemical structures of compound galactomannan.

**Table B.1:** Patent search document type.

| Year of publication | Document types     | Document type       | IPC Classifications* | Title                                                                                                                                                                                                                                                                                                                                                                                                    |
|---------------------|--------------------|---------------------|----------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2019                | Granted patent     | US 10308726 B2      | C08B37/00            | Chemistry metallurgy/organic macromolecular compounds their preparation or chemical working-up compositions based thereon/polysaccharides derivatives thereof/preparation of polysaccharides not provided for in groups Derivatives thereof cellulose                                                                                                                                                    |
|                     | Granted patent     | CN109673955-A       | A23L11/00            | Human necessities/foods or foodstuffs their treatment, not covered by other classes/foods, foodstuffs, or non-alcoholic beverages, not covered by subclasses or their preparation or treatment/pulses, i.e. fruits of leguminous plants, for production of fodder or food Products from legumes Preparation or treatment thereof                                                                         |
|                     | Granted patent     | BR102017027235-4 A2 | A23L33/21            | Human necessities/foods or foodstuffs their treatment, not covered by other classes/foods, foodstuffs, or non-alcoholic beverages, not covered by subclasses or their preparation or treatment/modifying nutritive qualities of foods Dietetic products Preparation or treatment thereof/Addition of substantially indigestible substances, e.g. dietary fibres addition of gelling or thickening agents |
|                     | Patent application | WO 2019/023685 A1   | D01D5/08             | Textiles paper/natural or man-made threads or fibres spinning/mechanical methods or apparatus in the manufacture of man-made filaments, threads, fibres, bristles or ribbons                                                                                                                                                                                                                             |
|                     | Granted patent     | CN 105853341 B      | A61K8/9789           | Human necessities/medical or veterinary science hygiene/preparations for medical, dental, or toilet purposes/cosmetics or similar toilet preparations                                                                                                                                                                                                                                                    |
| 2018                | Patent application | BRPI0925163         | B32B23               | Performing operations transporting/layered products/layered products, i.e. products built-up of strata of flat or non-flat, e.g. cellular or honeycomb, form/layered products essentially comprising cellulosic plastic substances                                                                                                                                                                       |
|                     | Patent application | BR102016027846-A2   | A21D13/062           | Human necessities/baking equipment for making or processing doughs doughs for baking/treatment, e.g. preservation, of flour or dough for baking, e.g. by addition of materials baking bakery products preservation thereof/finished or partly finished bakery products/Products with modified nutritive value/with modified sugar content Sugar-free products                                            |
|                     | Granted patent     | CN107913373-A       | A61K36/899           | Human necessities/medical or veterinary science hygiene/preparations for medical, dental, or toilet purposes/medicinal preparations of undetermined constitution containing material from algae, lichens, fungi or plants, or derivatives thereof, e.g. traditional herbal medicines/Poaceae or Gramineae (Grass family)                                                                                 |
|                     | Patent Application | BR102016021174-A2   | C10M109/02           | Chemistry metallurgy/petroleum, gas or coke industries technical gases containing carbon monoxide fuels lubricants peat/lubricating compositions/Lubricating compositions characterised by the base-material being a compound of unknown or incompletely defined constitution takes precedence                                                                                                           |
|                     | Patent application | BR102016026312      | A61K                 | Human necessities/medical or veterinary science hygiene/preparations for medical, dental, or toilet purposes                                                                                                                                                                                                                                                                                             |

Table B.1. Contd.

|      |                    |                     |            |                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                    |
|------|--------------------|---------------------|------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2017 | Patent application | CN 108606338 A      | A23N12/06  | Human necessities/foods or foodstuffs their treatment, not covered by other classes/machines or apparatus for treating harvested fruit, vegetables, or flower bulbs in bulk/Machines for cleaning, blanching, drying or roasting fruits or vegetables                                                                                                                                                                               | High-efficiency energy-saving <i>Adenanthera Pavonina</i> Linn washing equipment                                                                                                                                                                                                   |
|      | Patent application | BR102015021292-A2   | A01N65/20  | Human necessities/agriculture forestry animal husbandry hunting trapping fishing/preservation of bodies of humans or animals or plants or parts thereof/biocides, pest repellants or attractants, or plant growth regulators containing material from algae, lichens, bryophyta, multi-cellular fungi or plants, or extracts thereof containing compounds of determined constitution/Fabaceae or Leguminosae [Pea or Legume family] | Composition for controlling or combating larval form of <i>Aedes aegypti</i> mosquito which transmits yellow fever and dengue, contains proteinase inhibitor in aqueous solution which is extracted from seeds of <i>Adenanthera pavonina</i>                                      |
|      | Patent application | US 2018/0273649 A1  | C08B37/00  | Chemistry metallurgy/organic macromolecular compounds their preparation or chemical working-up compositions based thereon/polysaccharides derivatives thereof/preparation of polysaccharides not provided for in groups Derivatives thereof cellulose                                                                                                                                                                               | Crosslinked Polymer, Hydrogel Or Water-based Fracturing Fluid Comprising The Same, And Methods Of Making And Using Thereof                                                                                                                                                         |
|      | Patent application | BR102016013958      | A23J       | Human necessities/foods or foodstuffs their treatment, not covered by other classes/protein compositions for foodstuffs working-up proteins for foodstuffs phosphatide compositions for foodstuffs                                                                                                                                                                                                                                  | Produto alimentício à base de proteína vegetal e castanha de caju                                                                                                                                                                                                                  |
|      | Patent application | CN 106860825 A      | A61K31/045 | Human necessities/medical or veterinary science hygiene/preparations for medical, dental, or toilet purposes/medicinal preparations containing organic active ingredients                                                                                                                                                                                                                                                           | Traditional Chinese Medicine Ointment For Arthralgia Caused By Wind-damp-heat Pathogens, And Preparation Method Thereof                                                                                                                                                            |
|      | Patent application | BR102015017021-1 A2 | C09H05     | Chemistry metallurgy/dyes paints polishes natural resins adhesives compositions not otherwise provided for applications of materials not otherwise provided for/preparation of glue or gelatine/stabilisation of solutions of glue or gelatine                                                                                                                                                                                      | Produção de cola biodegradável a partir da semente de <i>adenanthera pavonina</i> l                                                                                                                                                                                                |
|      | Granted patent     | CN107281422-A       | A61K36/904 | Human necessities/medical or veterinary science hygiene/preparations for medical, dental, or toilet purposes/medicinal preparations of undetermined constitution containing material from algae, lichens, fungi or plants, or derivatives thereof, e.g. traditional herbal medicines/Stemonaceae ( <i>Stemona</i> family), e.g. <i>croomia</i> <i>Feedba</i>                                                                        | Ointment used to control tick in sheep, contains ivermectin tablets, <i>Fritillaria</i> , European grape fruit, <i>Viola</i> , <i>radix stemonae</i> , <i>herba gymnopteridis auriculatae</i> , <i>Chamaesium spatuliferum</i> , mulberry leaf, Chinese asafetida, bezoar and Aloe |
|      | Patent application | BR102015017019-A2   | A61K8/97   | Human necessities/medical or veterinary science hygiene/preparations for medical, dental, or toilet purposes/Cosmetics or similar toilet preparations/from algae, fungi, lichens or plants from derivatives thereof                                                                                                                                                                                                                 | Cream for treating hyperkeratosis, comprises galactomannan extracted from endosperm of <i>Adenanthera pavonina</i> and gel extracted from leaf of <i>Aloe barbadensis</i> homogenized in acetic acid                                                                               |
|      | Patent application | BR102015017020-3 A2 | C08B37/00  | Chemistry metallurgy/organic macromolecular compounds their preparation or chemical working-up compositions based thereon/polysaccharides derivatives thereof/preparation of polysaccharides not provided for in groups derivatives thereof cellulose                                                                                                                                                                               | Galactomannan is extracted from endosperm of <i>Adenanthera pavonina</i> , where galactomannan is cross-linked with glutaraldehyde to form network like structure                                                                                                                  |
|      | Patent application | CN 106819773 A      | A23L5/10   | Human necessities/foods or foodstuffs their treatment, not covered by other classes/foods, foodstuffs, or non-alcoholic beverages, not covered by subclasses or their preparation or treatment/general methods of cooking foods, e.g. by roasting or frying                                                                                                                                                                         | Method For Rapidly Cooking <i>Adenanthera pavonina</i> Plant                                                                                                                                                                                                                       |
|      | Patent application | BR102015024624-A2   | A01N31/08  | Human necessities/agriculture forestry animal husbandry hunting trapping fishing/preservation of bodies of humans or animals or plants or parts thereof/Biocides, pest repellants or attractants, or plant growth regulators                                                                                                                                                                                                        | Micro-capsules obtained from the nordestine biomass used for potential larvicide activity against the dengue transmitter mosquito, comprises unprecedented                                                                                                                         |

Table B.1. Contd.

|      |                    |                   |             |                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                              |
|------|--------------------|-------------------|-------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|      |                    |                   |             | containing organic oxygen or sulfur compounds                                                                                                                                                                                                                                                                                                                               | combination of aqueous solutions of natural polysaccharides as galactomannans                                                                                                                                                                |
|      | Patent application | CN 106615428 A    | A23F3/34    | Human necessities/foods or foodstuffs their treatment, not covered by other classes/coffee tea their substitutes manufacture, preparation, or infusion thereof                                                                                                                                                                                                              | Dendrobium Officinale Kimura Tea And Manufacture Method Thereof                                                                                                                                                                              |
|      | Granted patent     | CN107259906-A     | A47G9/10    | Human necessities/furniture domestic articles or appliances coffee mills spice mills suction cleaners in general/household or table equipment/pillows pillow holders                                                                                                                                                                                                        | Healthcare pillow useful for e.g. treating cervical spondylosis, premature ejaculation, insomnia and night sweats, comprises pillow structure which is filled with plant seed mixture containing black millet seed, grape seed and okra seed |
|      | Patent application | CN 106509606 A    | A23L11/00   | Human necessities/foods or foodstuffs their treatment, not covered by other classes/foods, foodstuffs, or non-alcoholic beverages, not covered by subclasses or their preparation or treatment/pulses, i.e. fruits of leguminous plants, for production of fodder or food Products from legumes Preparation or treatment thereof                                            | Cereals Capable Of Recuperating Constitutions Of Pregnant Women And Production Technology Of Cereals                                                                                                                                         |
|      | Patent application | BR102014023575-A2 | A61K36/185  | Human necessities/medical or veterinary science hygiene/preparations for medical, dental, or toilet purposes/medicinal preparations of undetermined constitution containing material from algae, lichens, fungi or plants, or derivatives thereof, e.g. traditional herbal medicines/Magnoliopsida (dicotyledons)                                                           | Obtaining galactomannan used for preparing galactomannan film, involves extracting Adenanthera pavonina seed endosperm                                                                                                                       |
|      | Granted patent     | CN105944041-A     | A61K36/9066 | Human necessities/medical or veterinary science hygiene/preparations for medical, dental, or toilet purposes/medicinal preparations of undetermined constitution containing material from algae, lichens, fungi or plants, or derivatives thereof, e.g. traditional herbal medicines/Curcuma                                                                                | Topical ointment useful for e.g. treating verruca plana, comprises honeysuckle, common andrographis herb, rhizoma coptidis, Conyza blinii, red paeony, Spatholobus stem, gallnut, cherry kernel, tuckahoe, oyster, Forsythia and licorice    |
| 2016 | Patent application | BR102014027289-A2 | A61K36/886  | Human necessities/medical or veterinary science hygiene/preparations for medical, dental, or toilet purposes/medicinal preparations of undetermined constitution containing material from algae, lichens, fungi or plants, or derivatives thereof, e.g. traditional herbal medicines/Aloeaceae (Aloe family)                                                                | Obtaining galactomannan used for preparing film for treating wound, involves utilizing Adenanthera pavonina seed endosperm powder                                                                                                            |
|      | Patent application | WO 2016/188446 A1 | C08B1/00    | Chemistry metallurgy/organic macromolecular compounds their preparation or chemical working-up compositions based thereon/polysaccharides derivatives thereof                                                                                                                                                                                                               | Crosslinked polymer, hydrogel or water-based fracturing fluid comprising the same, and methods of making and using thereof                                                                                                                   |
|      | Patent application | CN 105853341 A    | A61K8/97    | Human necessities/medical or veterinary science hygiene/preparations for medical, dental, or toilet purposes/cosmetics or similar toilet preparations                                                                                                                                                                                                                       | Anti-aging skincare product containing epidermal stem cell secretin and preparation method of anti-aging skincare product                                                                                                                    |
|      | Patent application | CN 105767934 A    | A23L15/00   | Human necessities/foods or foodstuffs their treatment, not covered by other classes/foods, foodstuffs, or non-alcoholic beverages, not covered by subclasses or their preparation or treatment/egg products preparation or treatment thereof                                                                                                                                | Honeysuckle Low-alkaline Preserved Egg And Preparation Method Thereof                                                                                                                                                                        |
|      | Granted Patent     | CN105441230-A     | C11D9/38    | Chemistry metallurgy/animal or vegetable oils, fats, fatty substances or waxes fatty acids therefrom detergents candles/detergent compositions use of single substances as detergents soap or soap-making resin soaps recovery of glycerol/compositions of detergents based essentially on soap compositions containing resin soap/products in which the composition is not | Tea oil cooling soap comprises e.g. composition A comprising e.g. tea oil extract, composition B comprising e.g. tea seed powder extract, composition C comprising e.g. Adenanthera pavonina extract, mountain spring water and brown sugar  |

Table B.1. Contd.

|      |                    |                |           |                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                          |
|------|--------------------|----------------|-----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|      | Patent application | CN 105441230 A | C11D9/02  | well defined<br>Chemistry metallurgy/animal or vegetable oils, fats, fatty substances or waxes fatty acids therefrom detergents candles/detergent compositions use of single substances as detergents soap or soap-making resin soaps recovery of glycerol                                                                                                                                  | Camellia Oil Cold Processed Soap                                                                                                                                                                                                         |
|      | Patent application | CN 105249160 A | A23L33/10 | Human necessities/foods or foodstuffs their treatment, not covered by other classes/foods, foodstuffs, or non-alcoholic beverages, not covered by subclasses or their preparation or treatment/modifying nutritive qualities of foods dietetic products preparation or treatment thereof                                                                                                    | Blood enriching and qi nourishing porridge                                                                                                                                                                                               |
|      | Patent application | CN 105249197 A | A23L33/00 | Human necessities/foods or foodstuffs their treatment, not covered by other classes/foods, foodstuffs, or non-alcoholic beverages, not covered by subclasses or their preparation or treatment                                                                                                                                                                                              | Health noodles                                                                                                                                                                                                                           |
|      | Granted patent     | CN104255531-A  | A01H4/00  | Human necessities/agriculture forestry animal husbandry hunting trapping fishing/new plants or processes for obtaining them plant reproduction by tissue culture techniques/lant reproduction by tissue culture techniques                                                                                                                                                                  | Method for breeding Adenanthera Pavonina, involves sterilizing Adenanthera Pavonina leaves, inoculating sterilized leaves into culture medium, and culturing embryogenic suspension cells followed by inducing embryonic cells and roots |
| 2015 | Patent application | CN 104861697 A | C09B61/00 | Chemistry metallurgy/dyes paints polishes natural resins adhesives compositions not otherwise provided for applications of materials not otherwise provided for/organic dyes or closely-related compounds for producing dyes mordants lakes fermentation or enzyme-using processes to synthesise a desired chemical compound                                                                | Formula used for preparing springgreen wheat straw dye and production method                                                                                                                                                             |
|      | Patent application | CN 104861693 A | B27K9/00  | Performing operations transporting/working or preserving wood or similar material nailing or stapling machines in general/processes, apparatus or selection of substances for impregnating, staining, dyeing or bleaching of wood, or for treating of wood with permeant liquids, not otherwise provided for chemical or physical treatment of cork, cane, reed, straw or similar materials | Formula used for preparing springgreen wheat straw dye and production method                                                                                                                                                             |
| 2014 | Patent Application | US20140045220  | C12Q1/68  | Chemistry metallurgy/biochemistry beer spirits wine vinegar microbiology enzymology mutation or genetic engineering/measuring or testing processes involving enzymes, nucleic acids or microorganisms immunoassay compositions or test papers therefor processes of preparing such compositions condition-responsive control in microbiological or enzymological processes                  | Composition for biosample treatment and method for nucleic acid amplification using the same                                                                                                                                             |
| 2013 | Granted Patent     | IN201103883-I4 | C08L00/00 | Chemistry metallurgy/organic macromolecular compounds their preparation or chemical working-up compositions based thereon/compositions of macromolecular compounds                                                                                                                                                                                                                          | Bioplastic composition used to obtain compostable bioplastic granules comprises biological waste which act as a prime ingredient; dilute hydrochloric acid; dilute sodium hydroxide; sodium hypochloride; and water                      |
|      | Granted Patent     | CN102719309    | A23D9/007 | human necessities/foods or foodstuffs their treatment, not covered by other classes/edible oils or fats, e.g. Margarines, shortenings, cooking oils/other edible oils or fats/characterised by ingredients other than fatty acid triglycerides                                                                                                                                              | Tea oil for reducing weight and processing technology                                                                                                                                                                                    |
|      | Patent Application | BR201104726-A2 | G01N33/52 | Physics/measuring testing/investigating or analysing materials by determining their chemical or physical properties/investigating or analysing                                                                                                                                                                                                                                              | Use of lectin-galactose binding molecule is claimed for diagnosing prostate diseases, where the lectin-                                                                                                                                  |

Table B.1. Contd.

|      |                    |                    |            |                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                            |
|------|--------------------|--------------------|------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|      |                    |                    |            | materials by specific methods not covered by groups                                                                                                                                                                                                                                                                                                                            | galactose binding molecule or frutalin utilizes<br>Artocarpus altilis seeds for treating prostatic basal cells                                                                                                                             |
|      | Patent application | US 2012/0294959 A1 | A01N65/20  | Human necessities/agriculture forestry animal husbandry hunting trapping fishing/preservation of bodies of humans or animals or plants or parts thereof                                                                                                                                                                                                                        | A Botanical Pesticide For Agriculture/horticulture Crops                                                                                                                                                                                   |
|      | Granted patent     | CN102416057-A      | A61K36/736 | Human necessities/medical or veterinary science hygiene/preparations for medical, dental, or toilet purposes/medicinal preparations of undetermined constitution containing material from algae, lichens, fungi or plants, or derivatives thereof, e.g. traditional herbal medicines/Prunus                                                                                    | Traditional Chinese medicinal composition, useful as a whitening composition, comprises Adenanthera pavonina, radix Angelica, Euphorbia lathyris leaf, cherry leaf and jasmine flower, prepared by e.g. crushing, soaking and spray drying |
| 2012 | Patent application | BR200910090-A2     | C08B37/00  | Chemistry metallurgy/organic macromolecular compounds their preparation or chemical working-up compositions based thereon/polysaccharides derivatives thereof/preparation of polysaccharides not provided for in groups Derivatives thereof cellulose                                                                                                                          | Method for obtaining galactomannan from Adenanthera pavonina, involves boiling seed of Adenanthera pavonina in distilled water and then seed is kept in order to swell                                                                     |
|      | Patent application | EP2531037          | A01N65/20  | Human necessities/agriculture forestry animal husbandry hunting trapping fishing/preservation of bodies of humans or animals or plants or parts thereof                                                                                                                                                                                                                        | A botanical pesticide for agriculture/horticulture crops                                                                                                                                                                                   |
|      | Patent application | AU 2011/210381 A1  | A01N65/20  | Human necessities/agriculture forestry animal husbandry hunting trapping fishing/preservation of bodies of humans or animals or plants or parts thereof                                                                                                                                                                                                                        | A botanical pesticide for agriculture/horticulture crops                                                                                                                                                                                   |
| 2011 | Patent application | WO 2011/092721 A1  | A01N65/20  | Human necessities/agriculture forestry animal husbandry hunting trapping fishing/preservation of bodies of humans or animals or plants or parts thereof                                                                                                                                                                                                                        | A botanical pesticide for agriculture/horticulture crops                                                                                                                                                                                   |
| 2010 | Granted patent     | EP 1850889 B1      | A61K8/73   | Human necessities/medical or veterinary science hygiene/preparations for medical, dental, or toilet purposes/cosmetics or similar toilet preparations                                                                                                                                                                                                                          | Depolymerized polysaccharide-based hydrogel adhesive and methods of use thereof                                                                                                                                                            |
| 2008 | Patent application | US 2008/0160118 A1 | A61K36/00  | Human necessities/ preparations for medical, dental, or toilet purposes                                                                                                                                                                                                                                                                                                        | Treatment of skin with cosmetic and dermatological preparations containing extracts from seeds of plants of the Genus Adenanthera                                                                                                          |
|      | Granted patent     | JP2007246429-A     | A61K36/18  | Human necessities/medical or veterinary science hygiene/preparations for medical, dental, or toilet purposes/medicinal preparations of undetermined constitution containing material from algae, lichens, fungi or plants, or derivatives thereof                                                                                                                              | New food/beverage products from an extract of one or more types of plants comprising preferably, Glirichidia sepium, useful in inhibiting lipase activity for decreasing blood triglyceride levels for treating obesity                    |
| 2007 | Patent application | JP 2007246429 A    | A23L1/30   | Human necessities/foods, foodstuffs, or non-alcoholic beverages, not covered by subclasses or their preparation or treatment                                                                                                                                                                                                                                                   | Lipase inhibitor, and food and drink                                                                                                                                                                                                       |
|      | Patent application | US 2007/0104676 A1 | A61K36/00  | Human necessities/ preparations for medical, dental, or toilet purposes                                                                                                                                                                                                                                                                                                        | Cosmetic and/or dermatological preparations containing an extract from the seeds of plants of the genus Adenanthera.                                                                                                                       |
| 2006 | Patent application | WO/2006/085329     | A61L15/60  | Human necessities/medical or veterinary science hygiene/methods or apparatus for sterilising materials or objects in general disinfection, sterilisation, or deodorisation of air chemical aspects of bandages, dressings, absorbent pads, or surgical articles materials for bandages, dressings, absorbent pads, or surgical articles/liquid-swellable gel-forming materials | Depolymerized polysaccharide-based hydrogel adhesive and methods of use thereof                                                                                                                                                            |
|      | Patent application | CA 2609790         | A61L15/60  | Human necessities/medical or veterinary science hygiene/methods or apparatus for sterilising materials or objects in general disinfection, sterilisation, or deodorisation of air chemical aspects of bandages, dressings, absorbent pads, or surgical articles materials for bandages, dressings, absorbent pads, or surgical articles/liquid-swellable gel-forming materials | Depolymerized Polysaccharide-based Hydrogel Adhesive And Methods Of Use Thereof                                                                                                                                                            |

Table B.1. Contd.

|      |                    |                   |           |                                                                                                                                                                                                                         |                                                                                                                            |
|------|--------------------|-------------------|-----------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
|      | Patent application | EP1635910         | A61K36/00 | human necessities/ preparations for medical, dental, or toilet purposes                                                                                                                                                 | Cosmetic and/or dermatological preparations containing an extract from the seeds of plants of the genus <i>Adenantha</i> . |
|      | Patent application | KR 20060028389 A  | A61K36/00 | Human necessities/ preparations for medical, dental, or toilet purposes                                                                                                                                                 | Cosmetic and/or dermatological preparations containing an extract from the seeds of plants of the genus <i>Adenantha</i> . |
| 2004 | Patent Application | WO 2004/100909 A1 | A61K36/00 | Human necessities/ preparations for medical, dental, or toilet purposes                                                                                                                                                 | Cosmetic and/or dermatological preparations containing an extract from the seeds of plants of the genus <i>Adenantha</i> . |
| 2002 | Granted Patent     | EP 1098991 B1     | C12N1/15  | Chemistry metallurgy/biochemistry beer spirits wine vinegar microbiology enzymology mutation or genetic engineering/microorganisms or enzymes compositions thereof/modified by introduction of foreign genetic material | Novel methods for the identification of ligand and target biomolecules                                                     |
|      | Granted Patent     | AU 751055 B2      | C12N1/15  | Chemistry metallurgy/biochemistry beer spirits wine vinegar microbiology enzymology mutation or genetic engineering/microorganisms or enzymes compositions thereof/modified by introduction of foreign genetic material | Novel methods for the identification of ligand and target biomolecules                                                     |
| 2000 | Patent Application | WO 2000/005406 A1 | C12N1/15  | Chemistry metallurgy/biochemistry beer spirits wine vinegar microbiology enzymology mutation or genetic engineering/microorganisms or enzymes compositions thereof/modified by introduction of foreign genetic material | Novel methods for the identification of ligand and target biomolecules                                                     |
|      | Patent Application | AU 1999/048985 A  | C12N1/15  | Chemistry metallurgy/biochemistry beer spirits wine vinegar microbiology enzymology mutation or genetic engineering/microorganisms or enzymes compositions thereof/modified by introduction of foreign genetic material | Novel methods for the identification of ligand and target biomolecules                                                     |