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A Systematic Review of *R. officinalis* L. Essential Oil: pharmacological properties and technological prospects

Revisão Sistemática do Óleo Essencial de Rosmarinus officinalis L.: propriedades farmacológicas e perspectivas tecnológicas

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Abstract

This study performs a systematic review of scientific and technological data on *Rosmarinus officinalis* essential oil (*Ro*-EO) and its application in nanostructured formulations. The research highlights the importance of nanotechnological delivery systems to increase solubility, prolong systemic circulation, and control drug release. The main constituents of *Ro*-EO include 1,8-cineole, α-pinene, and camphor. However, patent analysis has revealed a limited amount of technologies developed for nanoformulations containing *Ro*-EO. Since 2017, there has been a slowdown in Brazilian innovation related to *Ro*-EO, possibly due to less interest in new technologies related to essential oil. The reasons for this slowdown deserve further investigation, considering that *Ro*-EO already has commercial viability, due to its pharmacological properties and low toxicity, making it promising for future applications.

Keywords: Essential oil; *Rosmarinus officinalis;* Technological prospecting.

Resumo

Este estudo realiza uma revisão sistemática de dados científicos e tecnológicos sobre o óleo essencial de *Rosmarinus officinalis* (OE-*Ro*) e sua aplicação em formulações nanoestruturadas. A pesquisa destaca a importância dos sistemas nanotecnológicos de liberação para aumentar a solubilidade, prolongar a circulação sistêmica e controlar a liberação de fármacos. Os principais constituintes do OE-*Ro* incluem 1,8-cineol, α-pineno e cânfora. No entanto, a análise de patentes revelou uma quantidade limitada de tecnologias desenvolvidas para nanoformulações contendo o OE-*Ro*. Desde 2017, observou-se uma desaceleração na inovação brasileira, relacionada ao OE-*Ro*, possivelmente devido ao menor interesse em novas tecnologias relacionadas ao óleo essencial. As razões para essa desaceleração merecem investigação adicional, considerando que o OE-*Ro* já apresenta viabilidade comercial, devido às suas propriedades farmacológicas e à baixa toxicidade, tornando-o promissor para aplicações futuras.

Palavras-chave: Óleo essencial; *Rosmarinus officinalis*; Prospecção tecnológica.

Áreas Tecnológicas: Inovação e Desenvolvimento. Propriedade Intelectual. Propriedade Industrial.

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1 Introduction

The widespread observations on the use and efficacy of medicinal plants worldwide reinforce the practice of consuming herbal medicines and confirm the information collected over centuries (Mendonça; Silva-Mann; Rabbani, 2014). Nanoemulsions are colloidal dispersions at the nanoscale in which two immiscible solutions are dispersed in each other, creating a kinetically stable and long-lasting preparation (Laranjeira, 2016). They appear as transparent or translucent emulsions with droplet sizes ranging from 20 to 500 nm (Sneha; Kumar, 2022). However, according to Barkat *et al.* (2020), these particles should have a maximum size of 100 nm.

The nanoemulsion system consists of oil, water and specific surfactants and can be an oil-in-water (O/W) or water-in-oil (W/O) dispersion. One of its advantages is its ability to improve skin hydration and elasticity by better penetrating the stratum corneum. In addition, it can improve the permeability of poorly soluble active ingredients, provide a pleasant sensation, and spread better on the skin (Daudt *et al.*, 2013). Essential oils are usually obtained by hydrodistillation from the aerial parts of aromatic and medicinal plants, which are rich in various bioactive compounds such as mono- and sesquiterpenes (Aouadi *et al.*, 2021).

Rosmarinus officinalis L., commonly known as Alecrim in Brazil, is a widely distributed species in the Mediterranean region, including Morocco, France, and Spain (El Kharraf *et al.*, 2021). There is a growing interest in compounds from medicinal plants due to their high content of secondary metabolites with specific chemical properties that make them suitable for therapeutic purposes (Pérez-Mendoza *et al.*, 2020). This study aims to perform a comprehensive systematic review and technological prospection to collect scientific and technological data on *Rosmarinus officinalis* essential oil and its potential applications in nanostructured formulations.

1.1 Botanical Characteristics and Taxonomy of *Rosmarinus Officinalis*

Rosmarinus officinalis L., Taxonomic Serial n. 32.677 (ITIS, 2018), known in English as Rosemary, in Portuguese as Alecrim, and in Spanish as Romero, is an aromatic plant belonging to the family Lamiaceae, order Lamiales, class Magnoliopsida, and phylum Magnoliophyta (Borges *et al.*, 2019). This versatile plant thrives in dry or moderately moist soils and grows naturally in temperate climates. It is characterized by its linear and evergreen leaves, does not tolerate anaerobic or sodden soils and has moderate tolerance to salinity (Ribeiro-Santos *et al.*, 2015).

Rosemary is a shrubby plant, up to 2 meters in height with perennial green leaves, native to the Mediterranean region. It has an intense aroma and a bitter, astringent, and slightly spicy taste due to the chemical compounds contained in its essential oil, which accumulates in glandular trichomes (Kokkini; Karousou; Hanlidou, 2003; Ribeiro-Santos *et al.*, 2015).

1.2 Physicochemical Properties of the *Rosmarinus officinalis* Essential Oil (*Ro*-EO)

According to Carreiro *et al.* (2020), the main physicochemical tests for quality control of essential oils are the calculation of refractive index, absolute density and determination of chemical components by chromatography. This study performed a comparative analysis of the physicochemical aspects of commercial and laboratory-cultured (hydrodistilled) essential oils. The result was that there were no differences between the values of refractive index and absolute density when the commercial sample was compared with the cultured sample.

However, there were differences in the chemical composition of the main components, which is because the production of secondary metabolites is influenced by factors external to the plant, such as soil, climate, atmosphere, precipitation, parasite infestation, and so on (Simões *et al.*, 2017). The Brazilian Pharmacopeia characterizes the *Rosmarinus officinalis* essential oil (*Ro*-EO) as a colorless or slightly yellow-greenish liquid with a strong characteristic odor and aromatic, camphor-like and bitter taste, which must be stored under refrigeration in a hermetically sealed bottle protected from light (Brasil, 2010).

Table 1 – Some physicochemical properties of the *Ro*-EO

Relative density	0.894 - 0.912
Rotatory power	(-5) – (+15)
Refraction index	1.460 - 1.476
Acidity	< 1 %

Source: Adapted from Brasil (2010)

Atti-Santos *et al.* (2005) conducted a study on the *Ro*-EO from three harvests in 1998, 1999, and 2000. They found that α-pinene was the major component with 40-45% of the total oil components, followed by 1,8-cineole with 17-19%. The average density of the essential oil of the plants was 0.887 g/cm^3, with a refractive index of 1.489 and an optical rotation of +11.82°.

2 Methodology

The search was conducted using the following keywords: *Rosmarinus officinalis* essential oil, *Rosmarinus officinalis* essential oil and nanoformulation, *Rosmarinus officinalis* essential oil and nanoemulsion, which were almost identical for the academic papers and the patent search (with the additional inclusion of the terms nanoformulation and nanoemulsion for the patent search), considering all documents that contained this term in the title and/or abstract. The data were searched in June 2024 for records from 1979 to 2024 and then filtered and organized for further analysis.

Articles were sourced from the Portal de Periódicos da Coordenação em Aperfeiçoamento de Nível Superior (Capes), ScienceDirect (Elsevier), National Library of Medicine (PubMed), and Google Scholar databases were selected for data collection in scientific and technological bases. A search was also performed for patent applications at the Instituto Nacional de Propriedade Industrial (INPI), the World Intellectual Property Organization (WIPO), the European Patent Bank (EPO), and the United States Patent and Trademark Office (USPTO). All patent applications granted up to June 2024 were analyzed.

3 Results and Discussion

In this session, divided into four topics (bibliographic and patent survey), the main findings and results of the research will be presented and discussed, as well as their consequences in relation to the general objective proposed in this work.

3.1 The *Rosmarinus officinalis* Essential Oil and its Bioactive

The *Rosmarinus officinalis* essential oil contains an abundance of significant bioactive compounds, including monoterpene hydrocarbons (camphene, verbenene, α-pinene, β-pinene, limonene), oxygenated monoterpenes (1,8-cineole, linalool, camphor, borneol, verbenone), and sesquiterpenes (β-caryophyllene) (Sirocchi *et al.*, 2017). Monoterpenes, consisting of 10 carbon atoms, are derived from isoprene and are present in various essential oils (Borges *et al.*, 2019). These monoterpenes include 1,8-cineole (eucalyptol), a monoterpene oxide found in *Ro*-EO and other plant species (Sá; Andrade; Souza, 2013).

It has been shown to have inhibitory effects on experimental inflammation in rats, including carrageenan-induced paw edema, acetic acid-induced increase in peritoneal capillary permeability, and antinociception induced by intraplantar formalin and intraperitoneal acetic acid (Santos; Rao, 2000). In addition, studies by Lahlou *et al.* (2002) have shown that intravenous administration of 1,8-cineole induces hypotension in both anesthetized and conscious rats, suggesting a possible role in vascular relaxation. In addition, 1,8-cineole was found to directly block sodium channels in dissociated neurons from rat cervical ganglia, as reported by Ferreira-da-Silva *et al.* (2009).

According to Borges *et al*. (2019), 1,8-cineole is biosynthesized from α-terpineol by forming an ether bond between carbon atoms C1 and C8 and subsequent reduction. 1,8-cineole has been widely used as a promoter for the percutaneous action of various lipophilic drugs through the hairless skin of mice. In the study by Akbari *et al.* (2015), in which they investigated the effect of *Ro*-EO on the percutaneous absorption of topical diclofenac gel, a potentiating effect of 0.5–1% was demonstrated.

Further studies, such as those by Santos and Rao (2001), revealed gastroprotective effect of 1,8-cineole on ethanol-induced gastric mucosal injury in rats, significantly inhibited both gastric juice volume and total acid production. 1,8-cineole showed a tendency to restore the ethanol-associated decreases in non-protein sulfhydryls, suggesting a possible antioxidant effect.

In a study investigating the inhibitory effect of 1,8-cineole on cytokine production in cultured human lymphocytes and monocytes, a decrease in tumor necrosis factor-alpha (TNF-α) and Interleukin-1 beta (IL-1β) was observed, suggesting reduced effects on chemotactic cytokines. This is increasing evidence for the role of 1,8-cineole in controlling mucus hypersecretion in the airways by inhibiting cytokines, suggesting long-term treatment to reduce exacerbations in asthma, sinusitis, and chronic obstructive pulmonary disease (COPD) (Juergens *et al*., 2004).

The efficacy of 1,8-cineole in reducing inflammatory parameters is not limited to this study. Bastos *et al.* (2011) showed that treatment of ovalbumin-sensitized guinea pigs with inhaled 1,8-cineole reduced airway inflammatory parameters and provided evidence that the molecule was able to attenuate the development of airway hyperresponsiveness to carbachol in isolated rings, with reduced levels of tumor necrosis factor-alpha (TNF-α) and Interleukin-1 beta (IL-1β) in bronchoalveolar lavage. On the other hand, camphor is an oxygenated bicyclic monoterpene biosynthesized from borneol by oxidation of its hydroxyl group (Borges *et al*., 2019) and is also found in other genera of the Lamiaceae family such as the genus *Salvia*.

Tran *et al*. (2015) showed in their studies that the phytochemical component camphor attenuated the increase in senescence associated with β-galactosidase activity. The experiments showed that elastase decreased in human primary skin fibroblasts treated with camphor in a dose- and time-dependent manner, while the total amount of collagen increased. The results suggest that the compound is a potential healing and anti-wrinkle agent with considerable potential for use in cosmetics. Leite *et al*. (2007) investigated the inhibitory effects of β-pinene, α-pinene, and eugenol on the growth of gram-positive bacteria that can potentially cause infective endocarditis.

The study showed that the tested compounds effectively inhibited *Staphylococcus aureus*, *S. epidermidis*, *Streptococcus pneumoniae*, and *S. pyogenes*, demonstrating the antibacterial property of these phytochemicals. α-Pinene is a bicyclic monoterpene that, according to Borges *et al*. (2019), is the product of the electrophilic cyclization of α-terpineol, forming the pinyl cation that is deprotonated to form α-pinene.

In a study investigating the therapeutic efficacy of α-pinene in an experimental mouse model of ovalbumin-induced allergic rhinitis, α-pinene administration reduced levels of the pro-inflammatory cytokines TNF-α, IL -1β, and IL-6. It also decreased the mRNA expression of these cytokines and alleviated clinical symptoms such as nasal, ocular, and ear symptoms, as well as the infiltration of eosinophils and mast cells in nasal mucosal tissues, demonstrating its anti-inflammatory effect (Nam *et al*., 2014). Another study investigated the protective effect of α-pinene in mice with cerulein-induced acute pancreatitis.

Pretreatment with α-pinene significantly reduced the production of TNF-α, IL-1β, and IL-6 in the pancreas. Treatment with α-pinene also decreased pancreatic weight-body weight ratio, lowered amylase and lipase serum levels, and attenuated histological damage and myeloperoxidase activity in the pancreas and lungs (Bae *et al*., 2012). According to Borges *et al*. (2019), essential oil samples are classified into chemotypes based on their main constituents. *Rosmarinus officinalis* essential oil is classified as a cineole chemotype when its major constituent is 1,8-cineole, a camphor chemotype when camphor is the predominant constituent, and an α-pinene chemotype when α-pinene is the major constituent.

3.2 Pharmacological Activities of the *Ro*-EO and its Main Constituents

Cutrim *et al*. (2019) analyzed the *Ro*-EO, whose main constituents were camphor (37.00%), followed by 1,8-cineole (11.32%), and observed antimicrobial activity of *Ro*-EO against strains of *Escherichia coli and Staphylococcus aureus*. In the study by Pinto *et al*. (2019), *Ro*-EO, which was extracted by hydrodistillation, had 1,8-cineole as the main constituent at 42.11%, a (+)-2-bornanone at 16.37%, and α-pinene at 14.76%, and showed significant ovicidal activity on nematodes infesting sheep. *In vitro* tests showed that the oil inhibited between 97.4 and 100% of egg hatching and 20 to 74% of larval migration.

According to Minaiyan *et al*. (2011), *Ro*-EO, which was obtained by hydrodistillation and whose main components were α-pinene (39.8%) and 1,8-cineole (18.3%), proved to be effective in the treatment of sulfontrinitrobenzene-induced colitis in rats and showed anti-ulcerative and anti-inflammatory effects. According to Barreto *et al*. (2014), who studied the antimicrobial activity of *Ro*-EO and its possible antibiotic resistance-modifying effect in combination with other aminoglycoside antibiotics, a significant modulatory effect on drug resistance of *E. coli* and *S. aureus* strains was observed. The oil in question contained 1,8-cineole (30.87%), camphor (10.13%), and α-pinene (9.79%) as major components.

In another study investigating how *Ro*-EO can extend the shelf life of refrigerated beef under modified atmosphere, it was shown that packaging with *Ro*-EO under oxygen-rich conditions can extend shelf life by up to 15 days at a refrigeration temperature of 4 ºC (Sirocchi *et al*., 2017). Table 2 provides an overview of the main constituents of *Ro*-EO, the biological activity, the extraction method, the respective yields, as well as the place of collection of the plant material, and the location of the studies.

Table 2 – Main constituents of *Ro*-EO, activity, collection site, extraction method, yield and study site

Activity	Collection site	Major compounds	Extraction method	Yield	Reference
Antibacterial and antifungal	Sardinia (Italy)	α-pinene and borneol	Hydrodistillation	0.10 - 2.13 %	Angioni *et al*. (2004)
-	Tehran (Iran)	α-pinene and 1,8-cineole	Hydrodistillation	2.08 (m/m)	Nazari, Shaabani e Khiry (2011)
Antimicrobial	Castilla - La Mancha (Spain)	α-pinene and 1,8-cineole	Solvent-free microwave extraction	1.15 %	Moro *et al*. (2015)
Biological agents in control of pests	Heraklion (Greece)	camphor and 1,8-cineole	Hydrodistillation	-	Katerinopoulos *et al*. (2005)
Antifungal	Pelotas (Brazil)	camphor and 1,8-cineole	Hydrodistillation	3.4% (m/v)	Cleff *et al*. (2012)
Antibacterial and antifungal	Algeria	camphor and 1,8-cineole	Hydrodistillation	0.82 %	Djeddi *et al*. (2007)
Antibacterial, antifungal and antioxidant	Maranhão (Brazil)	camphor and 1,8-cineole	Hydrodistillation	0.3 (m/m)	Cutrim *et al*. (2019)
Coadjuvant agent in percutaneous absorption	Iran	α-pinene and 1,8-cineole	-	-	Akbari, *et al*. (2015)
Antifungal	Brazil	camphor and 1,8-cineole	Hydrodistillation	1.5 mL / 70 g	Da Silva Bomfim *et al*. (2015)
Antimicrobial	Brazil	camphor and 1,8-cineole	Steam distillation	-	Barreto *et al*. (2014)
-	Tehran (Iran)	α-pinene and 1,8-cineole	Hydrodistillation	2.05 %	Jalali-Heravi, Moazeni e Sereshti (2011)
Antimicrobial	Taizhou (China)	α-pinene and 1,8-cineole	Steam distillation	–	Jiang *et al*. (2011)
Antioxidant	Slovakia	α-pinene and 1,8-cineole	-	-	Horváthová, Slameňová e Navarová (2010)
Antioxidant and hepatoprotective effect	Belgrade	camphor and 1,8-cineole	Hydrodistillation	1.3% (v/m)	Rašković *et al*. (2014)
Ovicidal and larvicidal	Rio Grande do Sul (Brazil)	1,8-cineole and (+)-2-bornanone	Steam distillation	-	Pinto *et al*. (2019)
Antileishmanial and trypanocidal	Crato Seedling Production Bank (Brazil)	1,8-cineole and β-caryophyllene	Hydrodistillation	-	Pereira *et al*. (2017)

Source: Prepared by the authors of this article (2024)

The anti-inflammatory potential of *Ro*-EO has been researched by several authors. According to the study by Lorenzo-Leal *et al*. (2019), who tested the anti-inflammatory activity of *Ro*-EO using the anti-inflammatory cytokine IL-10 and the pro-inflammatory cytokines IL-6 and TNF-α, it was found that there was a fourfold increase in IL-10 compared to the untreated control, with no decrease in the number of pro-inflammatory cytokines, and anti-inflammatory activity was attributed to IL -10.

Takaki *et al* (2008) attributed the anti-inflammatory activity of *Ro*-EO to 1,8-cineole in synergy with myrcene. Juergens (2014) also suggested that 1,8-cineole acts through a mechanism of inhibition of 5 LOX (lipoxygenase) and COXs (cyclooxygenase) and prevents the formation of inflammatory arachidonic acid metabolites such as LTB 4 and PGE 2. The *Ro*-EO was also investigated for its antileishmanial and trypanocidal activity by Pereira *et al*. (2017). It was found that the oil not only has low toxicity, but also has clinically relevant antipromastigote and antitrypanosomal activity due to synergism between the components of the essential oil.

3.3 Nanostructured Systems Containing *Ro*-EO

Nanotechnology delivery systems offer promising advantages, such as improved solubility of hydrophobic drugs, prolonged systemic circulation, and delayed release, reducing the frequency of drug administration. These systems also minimize systemic side effects and allow simultaneous release of multiple drugs in combined therapies, promoting synergistic effects and preventing drug resistance (Allen Jr.; Popovich; Ansel, 2013). Extensive research has focused on the development of nanostructured formulations using *Ro*-EO.

This oil possesses various pharmacological activities, including antifungal, antibacterial, antihypertensive, antiproliferative, and antioxidant properties (Bomfim *et al*., 2015; Bonilla *et al*., 2016; Neves, 2020; Hussain *et al*., 2010). However, the oil is very unstable, especially in the presence of air, light, heat, moisture, and metals. It is susceptible to oxidation and volatilization (Simões *et al*., 2017).

Zibetti (2016) developed a stable nanoemulsion containing 5% *Ro*-EO by using a low-energy method called cold titration and phase inversion. The nanoemulsion, chemotype eucalyptol, showed excellent anti-herpes activity and remained stable throughout the study period of 60 days. It showed specific efficacy against herpes simplex serotype 2. Borges *et al*. (2019) studied the anti-inflammatory and analgesic activity of a *Ro*-EO -containing nanoemulsion with limonene, camphor, and 1,8-cineole as main components. The result was a potentiation of the effect of the essential oil, with efficacy demonstrated at a dose 600 times lower than the application of *Ro*-EO.

Pascual-Mathey *et al*. (2022) developed a nanoemulsion containing *Ro*-EO and investigated its protective effect against thioacetamide-induced hepatotoxicity. It was found that the nanoformulation significantly decreased the levels of alanine aminotransferase and aspartate aminotransferase compared to the non-derived oil. This proves that the nanoemulsified oil has a better hepatoprotective effect related to the change in the size of its antioxidant components.

3.4 Technological Prospecting

Table 3 shows the keywords that were searched for in the respective patent databases. There is no patent for a nanoformulation using *Rosmarinus officinalis* essential oil, although there are published articles on the preparation of a nanostructured formulation using *Ro*-EO. A search in ScienceDirect with the descriptors "essential oil *Rosmarinus officinalis* and nanoformulation" looking for an article from any year yielded no results, but a search in the same database with the descriptors "essential oil *Rosmarinus officinalis* and nanoemulsion" yielded eight articles.

A search with the keywords "essential oil *Rosmarinus officinalis* and nanoemulsion" in the subject line in the Capes Periodicals database yielded twenty-five articles. However, a search with the descriptors "essential oil *Rosmarinus officinalis* and nanoformulation" with the same search criteria yielded only two articles.

Table 3 – Number of patents found in INPI, EPO, USPTO and WIPO databases for the descriptors used

Keywords	INPI	EPO	USPTO	WIPO
Rosmarinus officinalis essential oil	4	5	1	65
Nanoformulation	5	29	11	112
Nanoemulsion	99	0	0	119
Rosmarinus officinalis essential oil and nanoformulation	0	0	0	0
Rosmarinus officinalis essential oil and nanoemulsion	0	0	0	0

Source: Prepared by the authors of this article (2024)

An analysis of the International Patent Classification (IPC) revealed that all patents found were registered in sections A (human needs), B (processing and transport operations), C (chemistry and metallurgy), or H (electricity), and each related to human needs, manufacturing processes, transportation, chemistry and metallurgy, and textiles and electricity. A search of WIPO's global technology database for the term "nanoemulsion" yielded no results, but a search for the Portuguese term "nanoemulsão" yielded 119 results.

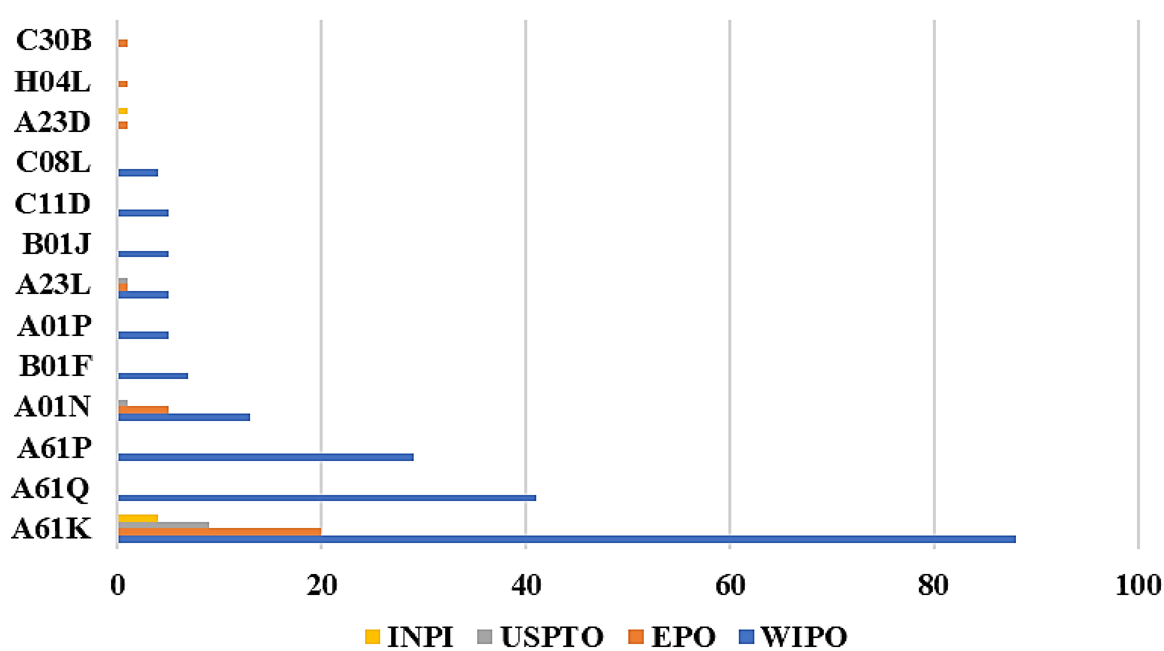
In addition, 73.94% of the patents belong to the international classification A61K, which covers human needs in medical and veterinary sciences with preparations for medical, dental or hygienic purposes. Figure 1 shows how the patents found in the WIPO, EPO, USPTO and INPI databases containing the term "nanoformulation" are distributed according to the international patent classification.

In the EPO database, of the total 29 patents found, 68.96% are classified as A61K, five patents are classified as A01N, which includes preservation of human or animal bodies or plants or parts thereof, biocides, herbicides, repellents or attractants for pests, and plant growth regulators, and the subclass includes compositions, physical forms, methods of using certain materials or of using individual compounds or compositions, one patent is classified as A23L, one as A23D covering edible oils or fats.

One as C30B covering, among other things, single crystal growth and unidirectional solidification of eutectic materials, and one as H04L covering basic electrical elements via waves using electromagnetic waves. In the USPTO technology database, of the 11 patents listed, 81.81% were classified as A61K, one as A01N, and another as A23L covering food, food products, or nonalcoholic beverages. Of the 5 patents found at INPI, 80% were classified as A61K and 20% as A23D.

Figure 2 shows the distribution of patents by country searched with the term "*Rosmarinus officinalis* essential oil" in the four databases. China had the most patents on "*Rosmarinus officinalis* essential oil", with a total of 43 patents. In the other countries, the number of published patents is much lower, with Japan, Korea, France and Brazil tied with 4 patents each.

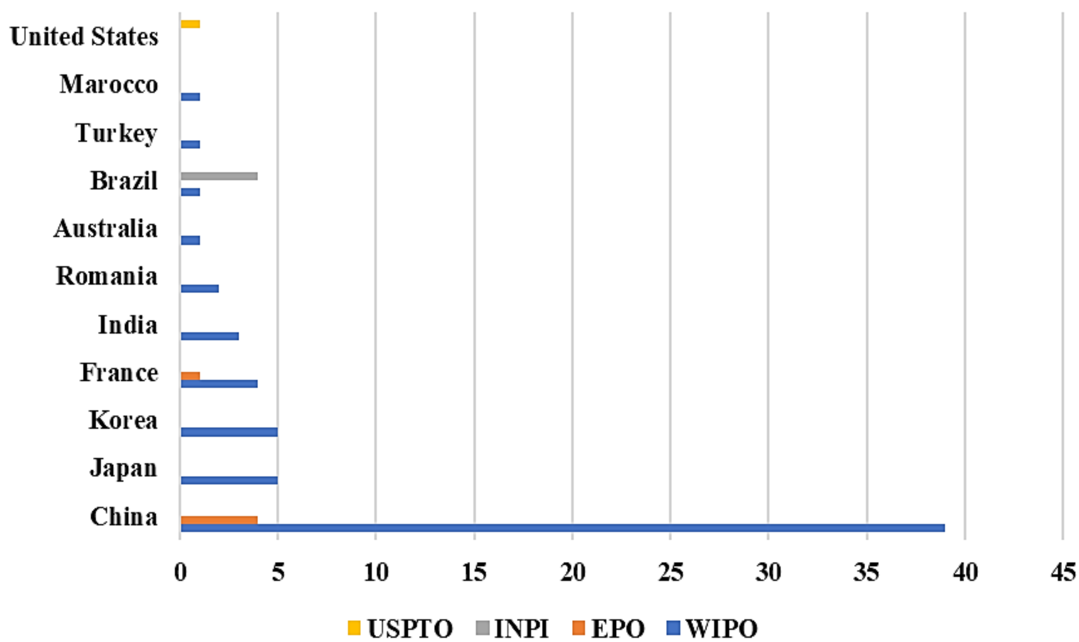
Figure 1 – Distribution of patents found over the term "nanoformulation" by international patent classification



Source: Prepared by the authors of this article (2024)

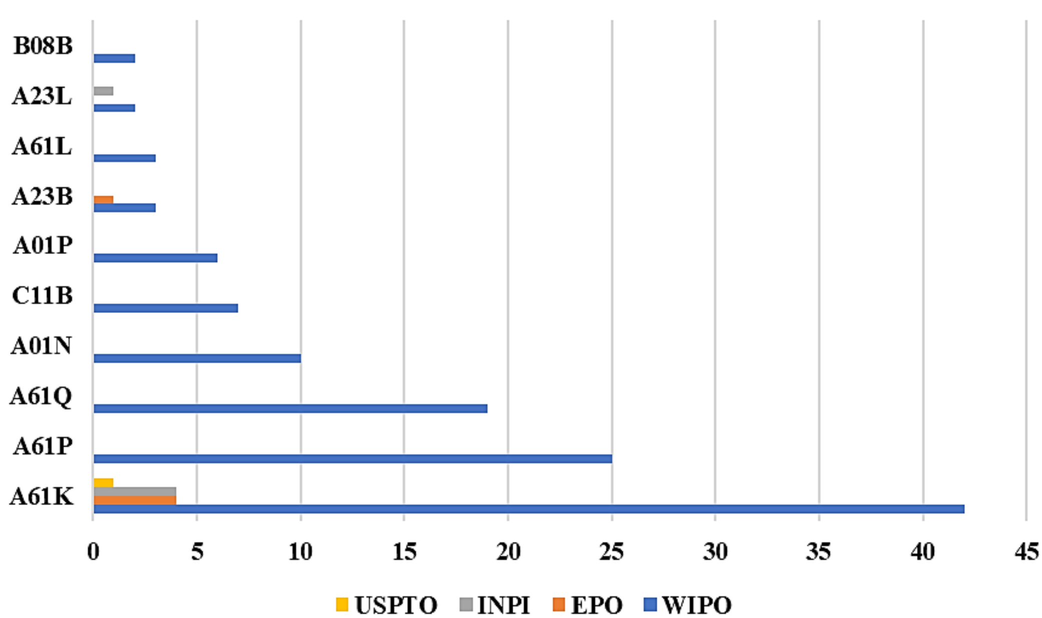
Figure 3 shows the number of patent applications according to the international patent classification. In the WIPO World Technology Database, 35% of patents are classified as A61K and 21% as A61P. In the other databases, most patents are also classified as A61K. For example, 80% of the *Rosmarinus officinalis* essential oil patents filed in the EPO database are classified as A61K, as are 80% in INPI and 100% in USPTO. One of the reasons for the higher number of patents related to *Ro*-EO with the classification A61K is the various studied and proven bio-pharmacological properties of this oil, of great interest to the pharmaceutical industry.

Figure 2 – Distribution of patents found using the term "*Rosmarinus officinalis* essential oil" by country in the four databases



Source: Prepared by the authors of this article (2024)

Figure 3 – Distribution of patents found using the term "*Rosmarinus officinalis* essential oil" by international patent classification



Source: Prepared by the authors of this article (2024)

Table 4 shows the data of patents filed for *Rosmarinus officinalis* essential oil in the INPI database to identify the inventions made in Brazil. Few patents have been filed at *Ro*-EO, although there are many studies on it, and that technological innovation with this oil has stagnated since 2017. It can also be noted that two of these patents were filed by universities, which shows that we are making slow progress in the production of patented formulations with *Ro*-EO.

Patent BR1020170254895 concerns the application of the essential oils of *Origanum vulgare* L. and *Rosmarinus officinalis* L. in the form of emulsions in foodstuffs as disinfectants as an alternative to chemical disinfectants with the aim of combating spoilage and pathogenic microorganisms by synergy between their subinhibitory concentrations. Patent BR1020170117537 concerns the use of a mixture of essential oils, which may consist of rosemary (*Rosmarinus officinalis*), carqueja (*Baccharis trimera*), lemon balm (*Lippia alba*), aloe (*Aloe vera*), barbatimão (*Stryphnodendron*) or a mixture thereof.

Patent application BR1020160276616 refers to a phytotherapeutic combination of the essential oils of *Rosmarinus officinalis*, *Juniperus Communis*, *Juniperus Virginiana*, *Amyris Balsamifera*, *Lavandula Angustifolia*, *Melaleuca Alternifolia* and *Eucalyptus Globulus*. This blend of oils acts synergistically to improve capillary follicle activity. Patent BR1020160276659 consists of a foaming solution used as a vehicle for solubilizing the minoxidil base, and in particular, a foaming solution used as a vehicle with a low alcohol concentration and capable of solubilizing the minoxidil base in a cold state up to a concentration of 7%.

The foaming solution of the invention consists of water, alcohol, the essential oils of *Rosmarinus officinalis*, *Juniperus Communis*, *Juniperus Virginiana*, *Amyris Balsamifera*, *Lavandula angustifolia*, *Melaleuca alternifolia*, *Eucalyptus globulus*, polyquaternium 10, glycerin, PEG -14m, acid lactic acid, PEG -40 castor oil, polysorbate 80, phenoxyethanol and sodium benzoate.

Analyzing the number of applications per year, we find that the first patent application for *Rosmarinus officinalis* essential oil was in 1979 (in the USPTO database) and the last one in 2021 (one patent), forty-three years ago. The years in which inventors began to protect technologies related to *Rosmarinus officinalis* essential oil, with 2017 being the year in which the most world patents were filed with WIPO, with a total of 11 patent applications (Figure 4).

In addition to the findings discussed, it is important to highlight the potential prospects of *Rosmarinus officinalis*. Despite the current stagnation in research and patent applications, new opportunities are emerging for the species. First, the increasing demand for natural and herbal products in various industries such as cosmetics, pharmaceuticals, and food offer an optimistic outlook for *Rosmarinus officinalis*. Its essential oil with its numerous bioactive compounds, holds promise for the development of innovative formulations and applications.

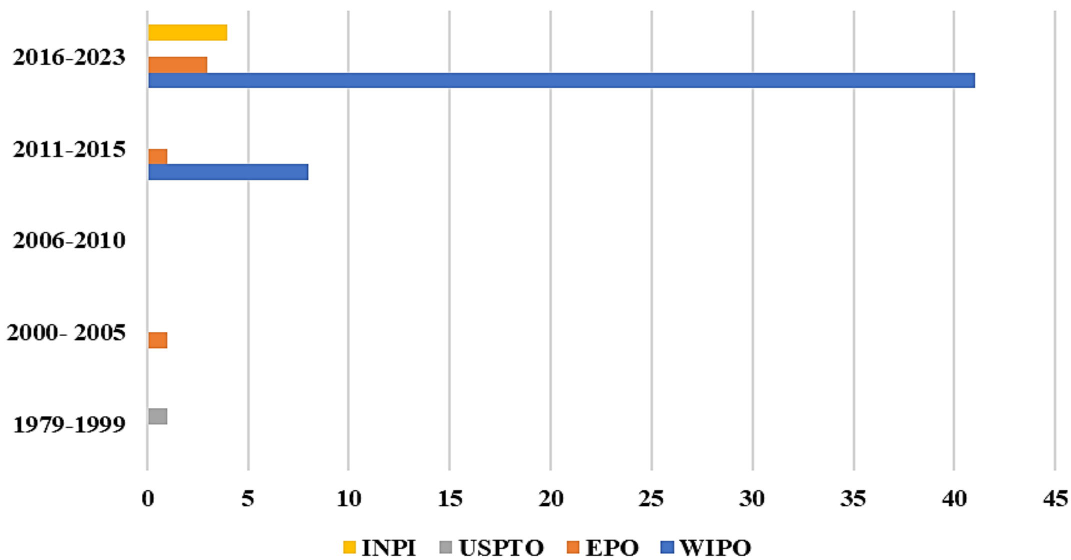
Moreover, the integration of nanotechnology with the properties of *Rosmarinus officinalis* essential oil offers exciting opportunities. Given the global focus on sustainable and environmentally friendly practices, the *Rosmarinus officinalis* species is consistent with the principles of green chemistry and sustainable agriculture. Its cultivation requires relatively low water consumption, making it suitable for regions with limited water resources.

Table 4 – Deposits of national patent applications in the INPI database filed under the term "Rosmarinus officinalis essential oil"

Patent Number	Patent Title	Patent depositor / year
BR1020170254895	Utilização de óleos essenciais de *Origanum vulgare L.* e *Rosmarinus officinalis L.*, em combinação sinérgica como sanitizantes de vegetais.	Universidade Federal da Paraiba (BR/PB)/2017
BR1020170117537	Composição e uso de composição no tratamento de endometrite em éguas	Fundação Universidade de Caxias do Sul (BR/RS)/2017
BR1020160276616	Combinação fitoterápica promotora da atividade de folículos capilares e composição farmacêutica para tratamento de alopecia.	SM Empreendimentos Farmacêuticos LTDA (BR/SP)/2016
BR1020160276659	Solução formadora de espuma utilizada como veículo para solubilização de Minoxidil base até 7%.	SM Empreendimentos Farmacêuticos LTDA (BR/SP)/2016

Source: Prepared by the authors of this article (2024)

Figure 4 – Patent applications found with the term "*Rosmarinus officinalis* essential oil" by year



Source: Prepared by the authors of this article (2024)

In addition, the use of *Rosmarinus officinalis* as a natural alternative in various industries reduces dependence on synthetic chemicals and promotes environmentally friendly practices. In summary, the future for *Rosmarinus officinalis* is promising despite the current challenges and stagnant research landscape. Expanding research efforts, exploring new applications and formulations, and capitalizing on the growing demand for natural products and sustainable practices can open new opportunities for this valuable species.

4 Final Considerations

In this study, we conducted a systematic review and technological exploration of *Rosmarinus officinalis* and its essential oil, focusing on its botanical characteristics, chemical composition, and pharmacological properties. The literature review highlights 1,8-cineole, α-pinene, and camphor as the most abundant and predominant compounds in *Rosmarinus officinalis* essential oil. Regarding technological progress, our investigation revealed a mismatch between the number of studies conducted on *Ro*-EO and the limited number of patents filed. Despite the great interest in nanotechnology, no patents have been filed to produce nanoformulations using *Ro*-EO.

In addition, our results indicate that studies on *Rosmarinus officinalis* essential oil in Brazil have stagnated since 2017. This indicates a lower interest in registering new technologies using *Ro*-EO, possibly due to decreased market potential and basic research in the country. Almost all the works that developed nanoemulsion with *Ro*-EO present an important challenge in their basic research in universities and other academic centers, to overcome the existing barriers between the original academic production and the productive activity - patent registration in regulatory bodies.

Although the results of the research in some cases are exceptionally promising, it is perceived that it is necessary not only the logic of producing scientific data in the form of articles but also the adoption of work logic and documentary records that guarantee the confidentiality of the protection and innovation in the intended patents, which in most centers does not exist. In our research, we can intuit that the teams of researchers in nanoemulsion development with *Ro*-EO are not sufficiently trained in the field of patent production and registration or do not have the necessary resources and legal tools for this purpose.

5 Future Prospects

As future perspectives, it is expected that new scientific research will be developed with the essential oil of *Rosmarinus officinalis* in association with the development of new formulations, since it is a species with potential for vast biopharmacological applications and with large cultivation in Brazil. The gap present in the area of patents related to the development of nanoformulations with *Ro*-EO points to an unexplored field for research. The application of nanotechnology offers promising opportunities for improving the efficacy and controlled delivery of *Ro*-

EO bioactive compounds, enabling its use in a variety of applications, such as treatments for chronic diseases, skin care, cosmetics, and the food industry. Therefore, exploiting the nanotechnological potential of *Ro*-EO would drive innovation in the pharmaceutical field and open up new commercial opportunities.

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