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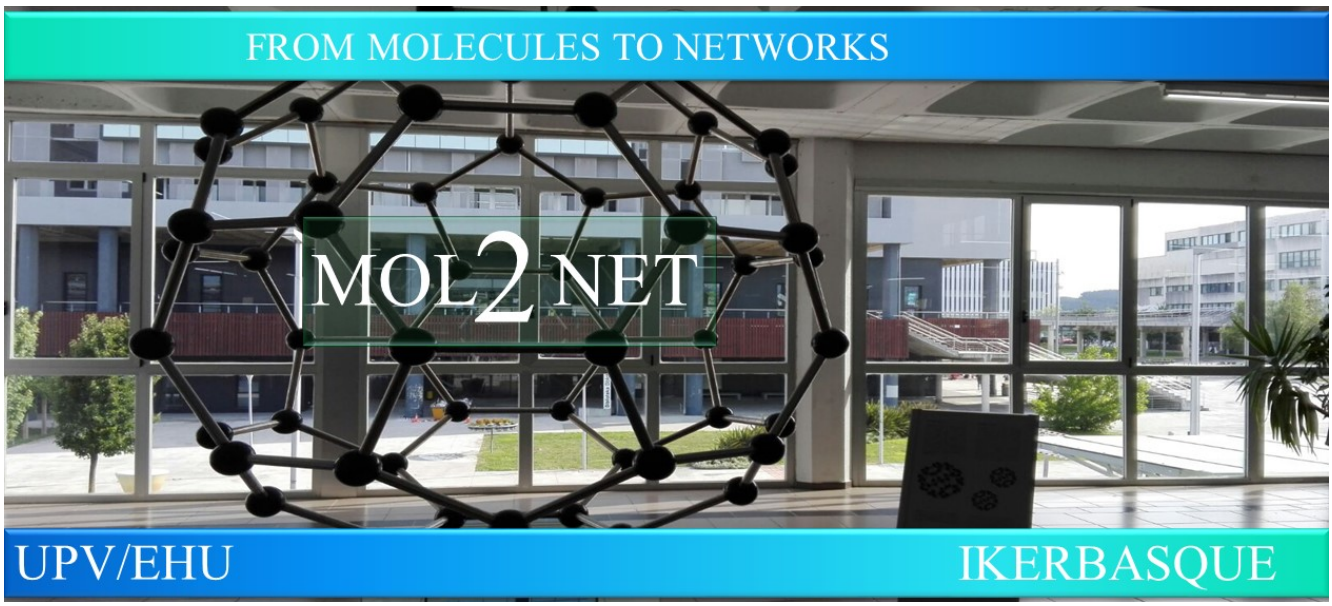

Use of chemical compound searches to study the patentability of rosmarinic acid

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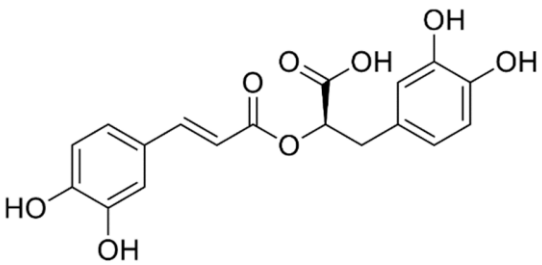
Graphical Abstract



Abstract.

This study, in the form of a patent analysis, presents the state by introducing what has been innovated and patented concerning rosmarinic acid. Furthermore, a detailed analysis of the patentability, using the "chemical compounds search" of the Patentscope database, has been provided regarding publication years, applicants, jurisdictions, and patent classifications.

Keywords: *rosmarinic acid; Rosmarinus officinalis; chemical compounds search; patentability; patent analysis.*

Introduction

Rosmarinic acid (RA) is a phenolic compound that occurs naturally in many higher plants, particularly Lamiaceae. The name of this acid is based on the plant's name from which it was first isolated, *Rosmarinus officinalis*, by chemists Scarpati and Oriente [1]. RA is an ester of caffeic acid and 3,4-dihydroxyphenyl lactic acid. Its chemical formula is $C_{18}H_{16}O_8$ and its molecular weight is 360.3164 $g.mol^{-1}$ [2]. It can be extracted from plant material by solid-liquid extraction using organic solvents such as methanol, ethanol, and acetone [3]. Other extraction methods were used, such as maceration, heat reflux, and Soxhlet extraction; however, their extraction yield was low [4].

Since rosmarinic acid has several biological activities, it has been very useful for pharmaceutical, cosmetic, and food applications [5]. Indeed, it has been revealed that the inhibitory effect of RA against acetylcholinesterase is promising for the treatment of neurodegenerative diseases [6]. The anti-inflammatory effect of RA has also been documented. It is probably due to the inhibition of lipoxygenases and cyclooxygenases and the interference of rosmarinic acid with the complement cascade [7]. RA has several other activities, including antioxidant, antibacterial, hepatoprotective, and cardioprotective properties [8]. Nadeem *et al.* recently conducted a review on the therapeutic benefits of RA and identified those mentioned above in addition to the effects against allergies, cancer, diabetes, and depression, as well as the nephroprotective effect, while concluding that the precise mechanism of action of RA deserves more research (**Figure 1**) [9].

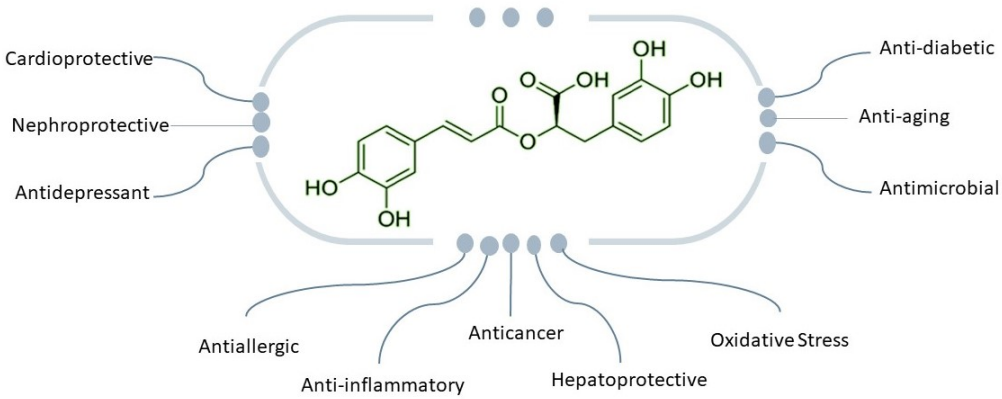


Figure 1. *The structure of rosmarinic acid and its bioactivities(Adapted from Nadeem et al., 2019 [9]. Copyright © 2019 MDPI under the terms of the Creative Commons Attribution 4.0 International License).*

As a source of production of drugs, food complements, and natural products, research and development in this area of RA is developing rapidly through the innovation and improvement of raw materials, chemical synthesis, methods of preparation, formulations, and fabrication processes, as well as applications. This is also evident from the increase in the number of patent applications filed worldwide each year in this area of research and development. Use of patent information to characterize innovation and trends in this area of RA could lead to various recommendations and may help one to plan and innovate a research strategy [10-13]. This study concerns the analysis of international patent applications on the RA molecule through the Patent Cooperation Treaty (PCT) global system. More specifically, this study presents the patentability study of the RA molecule by introducing what has been innovated and patented. It is established as a research planning tool in accordance with patent analysis standards [14-17]. Furthermore, a detailed analysis is provided regarding publication years, applicants, jurisdictions, and patent classifications by using the "Chemical Compounds Search" of the Patentscope database.

Materials and Methods

The patents of the RA molecule studied hereinafter were based on the "Chemical Compounds Search" of the Patentscope database [18]. It is a search service provided by the World Intellectual Property Organization (WIPO) [19]. The chemical structure search recognizes the names of chemical compounds in patent texts and their structures from the embedded drawings. Briefly, this tool standardizes all the different representations of chemical structures into the International Chemical Identifier (InChI). This is a textual identifier developed to make it easy to perform web searches for chemical structures [20]. Also, InChIKey is another parameter that could be used for the chemical structure search. InChIKey is a fixed-length (27-character) condensed digital representation of an InChI. It provides a precise, robust, and approved structure-derived tag for a chemical substance [21]. The RA molecule's information used in this study is shown in **Table 1**.

Table 1. *The queries used in this study: InChI, InChiKey, molecular formula, and molecular weight.*

Molecule	Rosmarinic acid or alpha-(((3,4-Dihydroxyphenyl)-1-oxo-2-propenyl)oxy)-3,4-dihydroxybenzenepropanoic acid
InChI	1S/C18H16O8/c19-12-4-1-10(7-14(12)21)3-6-17(23)26-16(18(24)25)9-11-2-5-13(20)15(22)8-11/h1-8,16,19-22H,9H2,(H,24,25)/b6-3+/t16-/m1/s1
InChIKey	DOUMFZQKYFQNTF-WUTVXBCWSA-N
Molecular formula	$C_{18}H_{16}O_8$
Molecular weight	360.3164 g.mol^{-1}

Results and Discussion

Based on definitions of the terms used generally in the world of patent information, publication is the step when the patent document (patent application, granted patent, etc.) is made available to the public, to which a publication number and a publication date have been assigned by a patent authority. In other words, the publication date is the date on which a patent document is published, thereby making it part of the state of the art [10-13]. **Figure 2** presents the publication years of the resultant patents for the RA molecule.

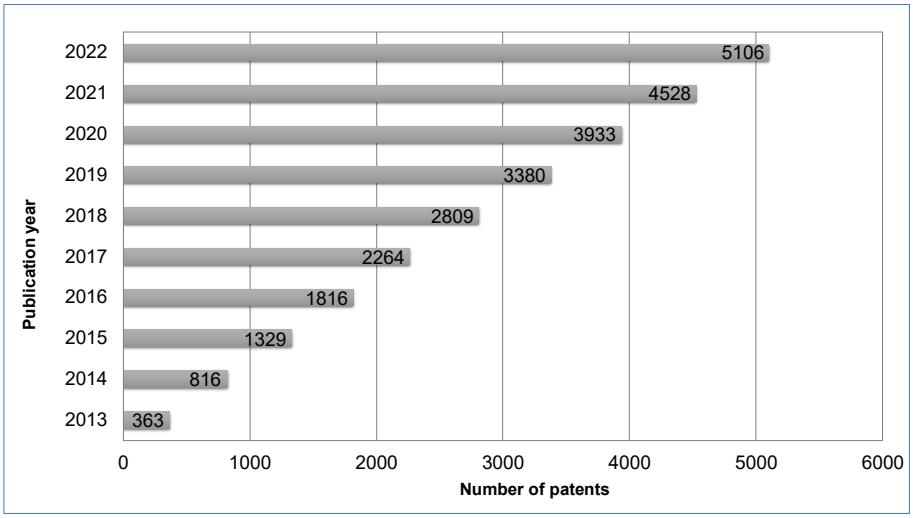


Figure 2. *Publication years of resultant patents for the RA molecule.*

An applicant is a person (i.e., a natural person) or an organization (i.e., a legal entity) that has filed a patent application. In several cases, the applicant can also be the inventor, and there may be more than one applicant per patent application. [10-13]. **Figure 3** depicts the top ten applicants for the RA molecule's resulting patents.

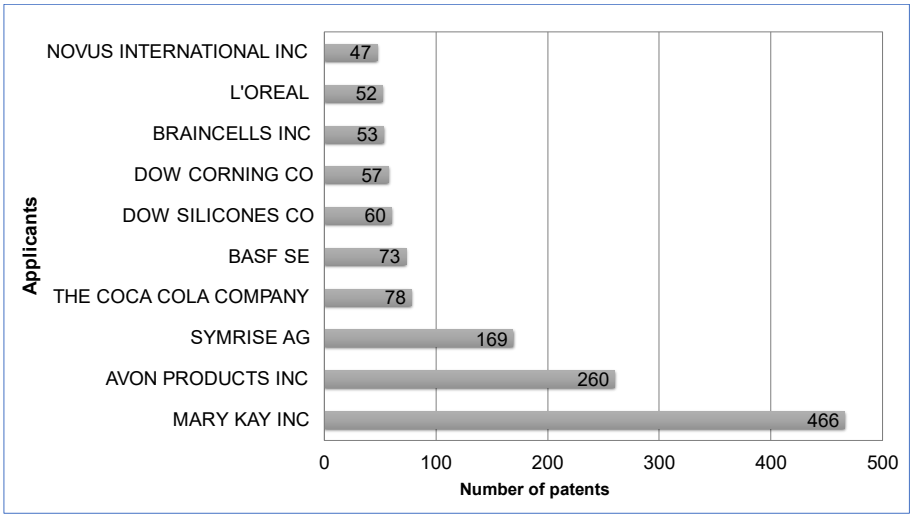


Figure 3. *Applicants (top 10) of resultant patents for the RA molecule.*

An applicant, or first-mentioned applicant in the case of joint applicants, can file an application for a patent at the appropriate patent office under whose jurisdiction he normally resides, has his domicile, has a place of business, or the place from where the invention actually originated. If patent protection is sought in a number of countries worldwide, an applicant may consider filing an international application under the PCT global system [22]. **Figure 4** presents the top ten jurisdictions of resultant patents for the RA molecule.

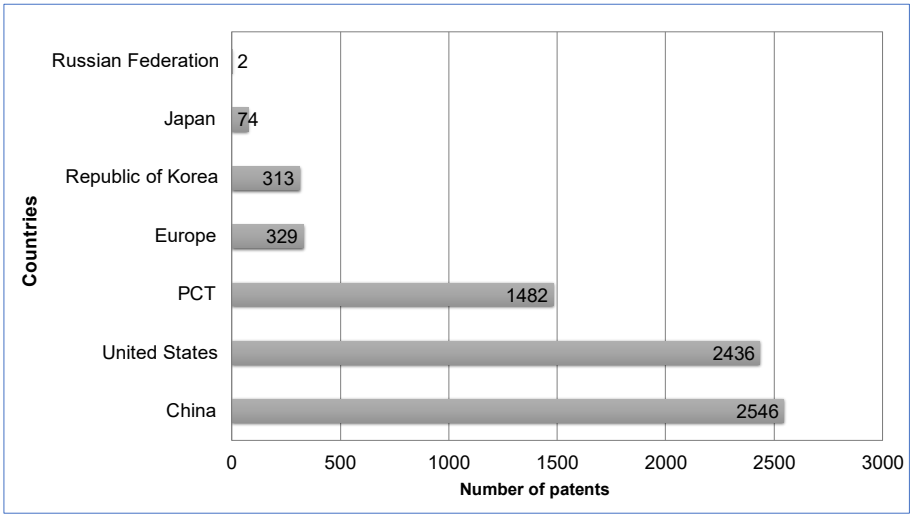


Figure 4. *Jurisdictions (top 10) of resultant patents for the RA molecule.*

The International Patent Classification (IPC) is a hierarchical system in the form of codes, which divides all technology areas into a range of sections, classes, subclasses, groups, and subgroups [23]. It is an international classification system that provides standard information to categorize inventions and to evaluate their technological uniqueness [24]. For RA molecule, the top 10 IPC codes are presented in **Figure 5**. These IPC codes concern only patent applications under PCT global system. The most common IPC code for RA molecule patents corresponds to A61K, which is a subclass meaning

preparations for medical, dental, or toilet purposes. This subclass has recorded it alone 5523 patents. Secondly, the subclass A61P that defines the specific therapeutic activity of chemical compounds or medicinal preparations has recorded 2215 patents. Thirdly, the subclass A61Q, which means the specific use of cosmetics or similar toilet preparations, has recorded 2033 patents. For more details concerning these top ten, a description of each IPC code is shown in **Table 2**.

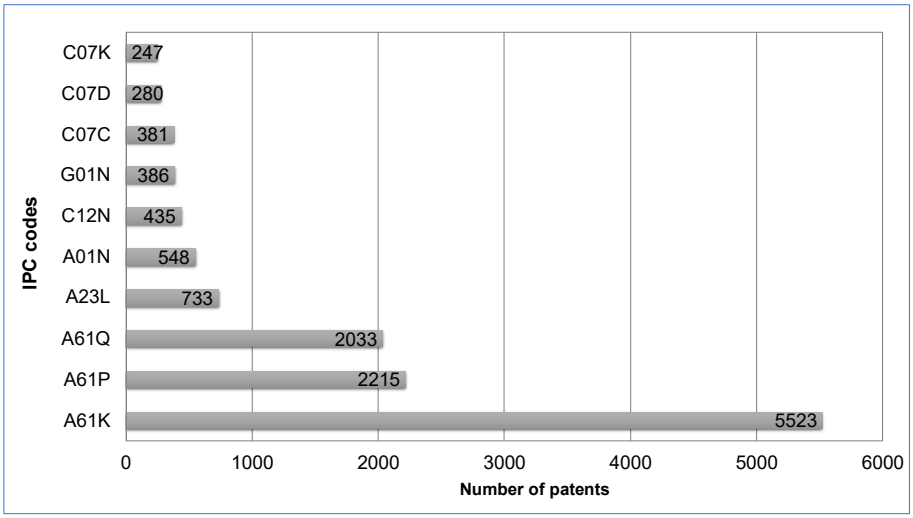


Figure 5. *IPC codes (top 10) of resultant patents for the RA molecule.*

Table 2. *Description of patent classifications concerning the resulting patents of the RA molecule [23].*

IPC	Description
A61K	Preparations for medical, dental, or toilet purposes.
A61P	Specific therapeutic activity of chemical compounds or medicinal preparations.
A61Q	Specific use of cosmetics or similar toilet preparations.
A23L	Foods, foodstuffs, or non-alcoholic beverages.
A01N	Preservation of bodies of humans, animals, plants, or parts thereof.
C12N	Microorganisms or enzymes; compositions thereof; propagating, preserving, or maintaining microorganisms; mutation or genetic engineering; culture media.
G01N	Investigating or analyzing materials by determining their chemical or physical properties.
C07C	Acyclic or carbocyclic compounds.
C07D	Heterocyclic compounds.
C07K	Peptides.

Conclusions

During our search, we found 5016 patent documents. China was ranked first with 2546 patent documents, followed by the United States with 2436 patent documents. The innovation and improvement of RA are concerned with raw materials, synthesis, and methods of preparation, as well as formulations and fabrication processes. Based on the patent classification codes, all granted patents and most inventions are intended for preparations for medical, dental, or toilet purposes and specific therapeutic activity of chemical compounds or medicinal preparations, as well as specific use of cosmetics or similar toilet preparations. According to knowledge clusters and expert driving factors, research based on the preservation of the bodies of humans, animals, and plants is concentrated in the majority of patents.

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