

Analysis of uses of essential oils and terpenics/terpenoids compounds by pharmaceutical industry through USPTO granted patents

SILVA-SANTOS, A.^{1*}; ANTUNES, A.M.S.²; BIZZO, H.R.³; d'AVILA, L.A.²; SOUZA-SANTOS, L.C.⁴; SOUZA, R.C.⁴

¹ D.Sc.; Patent Examiner from Brazilian Institute of Industrial Property (INPI), Praça Mauá, nº 07, CEP: 20081-900, Rio de Janeiro, Rio de Janeiro, Brazil. * adailson@inpi.gov.br; adsantos2005@yahoo.com.br ² D.Sc.; Department of Organic Processes at Escola de Química da Universidade Federal do Rio de Janeiro (EQ/UFRJ). Av. Brigadeiro Trompowski s/n, Centro de Tecnologia - Bloco E, CEP: 21949-900, Rio de Janeiro, Rio de Janeiro, Brazil. E-mails: davila@eq.ufrj.br; adelaide@eq.ufrj.br ³ D.Sc.; Researcher of Embrapa Agroindústria de Alimentos (CTAA/EMBRAPA), Av. das Américas, 29501, CEP: 23020-470, Rio de Janeiro, Rio de Janeiro, Brazil. E-mail: bizzo@ctaa.embrapa.br ⁴ Escola de Engenharia da Universidade Federal Fluminense (UFF), Campus Praia Vermelha, R. Passo da Praia, 156, São Domingos, 24210-005, Niterói, Rio de Janeiro, Brazil. E-mails: leilacsantos@yahoo.com.br; quel_cs@yahoo.com.br

ABSTRACT: In the area of drugs development, natural products represent a myriad of templates for new lead medicines. This work identifies the uses of essential oils and terpenics/terpenoids compounds by pharmaceutical industry through the granted patents databank from United States Patent and Trademarks Office. One-thousand-two-hundred-ninety-eight documents have been listed between 1980-2003 years. The most important pharmaceutical uses of essential oils and terpenics/terpenoids compounds are as dermatological, antibiotics, analgesics, anti-inflammatory, neurological, gastrointestinal, heart diseases and anticancer areas.

Key words: essential oils, terpenes, patents, pharmaceutical industry, technological forecasting

RESUMO: Análise da utilização dos óleos essenciais e compostos terpênicos/terpenóides pela indústria farmacêutica através das patentes concedidas pelo Escritório Norte-americano de Marcas e Patentes (USPTO). Na área do desenvolvimento de fármacos, produtos naturais são uma incrível fonte de inspiração para a obtenção de novas entidades químicas e/ou medicamentos. Este trabalho identificou a utilização de óleos essenciais e compostos terpênicos/terpenóides pela indústria farmacêutica mundial através das patentes concedidas pelo Escritório Norte-americano de Marcas e Patentes (USPTO). Listou-se 1.298 documentos entre os anos de 1980-2003. As utilizações dos óleos essenciais e compostos terpênicos/terpenóides farmacêuticas mais importantes estão nas áreas dermatológica, antibiótica, anagésica, antiinflamatória, neurológica, gastrointestinal, doenças do coração e anticancerígenas.

Palavras-chave: óleos essenciais, terpenos, patentes, indústria farmacêutica, prospecção tecnológica

INTRODUCTION

Plants synthesize the majority of known organic substances that are used for the treatment of illnesses that charged the humanity (Reinbothe et al., 1990). Two examples are cancer and infectious diseases treatment, where over 60% and 75% of the drugs developed come from vegetable sources (Newman et al., 2003). Amongst plants metabolites,

essential oils and their terpenics/terpenoids compounds are characterized as the main chemical compounds to be isolated and used by man (Craveiro & Queiroz, 1993; Silva-Santos et al., 2004; Montanari & Bolzani, 2001; Joulain, 1993).

The global market of pharmaceutical products represents 33% of world-wide chemical compounds

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production (Newman et al., 2003, *op.cit*) and motivated by the reduction of costs in research and development (R&D) activities, the most important pharmaceutical companies (Seidl, 2002) are investing in bioprospective research to find new compounds to synthesize new lead medicines. To protect these investments, patents are the main mechanism used by them, playing an important role in R&D programs for the development of pharmaceutical products in developed countries (Lozano, 2002; Araújo, 1984).

Besides the technological forecast has great importance and extreme worth for companies and governments nowadays, been characterized as a continuous process that try to foresee situations and environments at the same time that provides subsidies to take decisions that will be more correct and

adjusted (Archibugi & Michie, 1995).

This work aims to show the relevance of elaborating a database consisting of patents (USPTO, 2002/2004; Wilson, 1987) through a study between 1980-2003, about the pharmaceutical uses of essential oils and terpenics/terpenoids compounds, becoming possible the identification of technological areas, owners, inventors, varieties of essential oils, terpenics/terpenoids, etc.

METHODOLOGY

The databank was made by the keyword (essential oil(s), terpenic(s) and terpenoid(s)) search mechanism in the fields of 'Claims' and 'Abstract' of USPTO (United States Patent and Trademarks Office) granted patents documents. The technological

TABLE 1. Groups of International Patent Classification related with the use of essential oils and terpenics/terpenoids compounds in the pharmaceutical sector

Groups of IPC	Discrimination
A61K 6/00	Dental preparations
A61K 9/00	Medicinal preparations characterized by special physical form
A61K 31/00	Medicinal preparations containing organic active ingredients
A61K 35/00	Medicinal preparations containing material or reaction products thereof with undetermined constitution, like extracts of plant
A61K 47/00	Medicinal preparations characterized by the non-active ingredients used, e.g. carriers, inert additives

knowledge for the use of essential oils and terpenics/terpenoids compounds in the pharmaceutical sector is indexed by the International Patent Classification (IPC) (WIPO, 2002/2004) in Subclass A61K (Preparations for medical, dental, or toilet purposes), pertaining to Section A (Human Necessities) of IPC, through the groups listed in the following Table 1.

Also it has been established a methodology of analysis of documents, combining bibliographical information from patents, like 'cover page', 'abstract' and 'claims' fields, capable to identify the following items: a) Historical series; b) Essential oils; c) Terpenics Compounds; d) Terpenoids Compounds; e) Nature and nationality of the owners of patents rights; f) Identification of the main owners and g) Application that destines the invention.

RESULT AND DISCUSSION

For the period of 1980-2003, had been found 1,298 patents (Figure 1). Figure 2 details the distribution of patents across the five groups of the IPC showed in Table 1 and also detaches the main sub-groups for each one.

The predominance for the application of essential oils and terpenics/terpenoids compounds have been as active ingredients for the therapeutical

action in the following groups: Dental preparations (A61K 6/00), Medicinal preparations containing organic active ingredients (A61K 31/00) and Medicinal preparations containing material or reaction products thereof with undetermined constitution, like extracts of plants (A61K 35/00), and, partially, Medicinal preparations characterized by special physical form (A61K 9/00). On the other hand, as non-active or complementary ingredients, the uses of essential oils and terpenics/terpenoids compounds are characterized by the group A61K 47/00 (Medicinal preparations characterized by the non-active ingredients used, e.g. carriers, inert additives) and A61K 9/00 (Medicinal preparations characterized by special physical form).

The application of essential oils and terpenics/terpenoids compounds as pharmaceutical active ingredients was indexed by: A61K 6/02 preparations dentistry for artificial teeth, for filling or for capping teeth; A61K 31/33 - Medicinal preparations containing Heterocyclic compounds like organic active ingredients; A61K 9/10, about Medicinal preparations characterized by special physical form like Dispersions or Emulsions; A61K 9/14 - Medicinal preparations characterized by special physical form like Particulate Material; A61K 9/20 - Medicinal

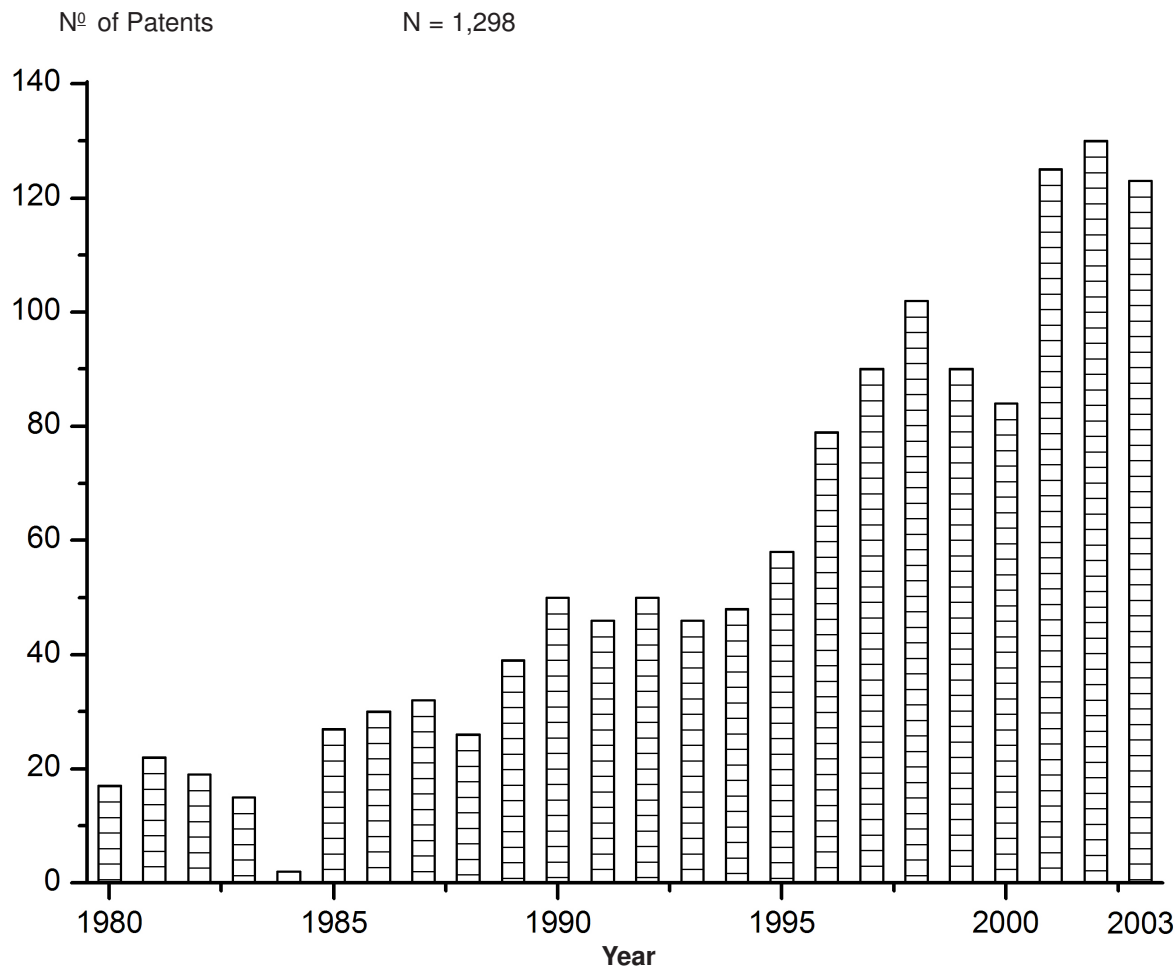


FIGURE 1. USPTO granted patents for the use of essential oils, terpenics/terpenoids compounds in the pharmaceutical sector between 1980-2003.

preparations characterized by special physical form like Pills, lozenges or tablets; A61K 31/185 - Medicinal preparations containing Acids, Anhydrides, halides or salts thereof like organic active ingredients; A61K 31/70 Medicinal preparations containing Carbohydrates, Sugars, Derivatives thereof like organic active ingredients; A61K 35/78 - Medicinal preparations containing Materials from plants or reaction products thereof with undetermined constitution; and A61K 47/46 - Medicinal preparations containing ingredients of undetermined constitution or reaction products thereof characterized for being non-active ingredients. Figure 3 detailed the areas where essential oils and terpenics/terpenoids compounds were used.

The register of use of essential oils in patents was indexed by groups A61K 6/00, A61K 9/00, A61K 35/00 and A61K 47/00, and their corresponding sub-groups. The application of terpenes and terpenoids are centered in group A61K 31/00 (and its sub-groups).

Essential oils and terpenics/terpenoids compounds

The matter identified in the '*abstract*' and '*claims*' disclose that amongst essential oils, 15 had answered by 94.31% of 1,564 registered bibliographical citations: a) condimentous essential oils (sesame, clove, ginger, pepper, garlic), 599 citations; b) citrus essential oils (orange, lemon, grapefruit and bergamot), with 376; c) mints essential oils (peppermint and spearmint), 214 citations; d) essential oils extracted from pine and eucalyptus, respectively, with 129 and 73 citations; and e) floral essential oils (rose and rosemary), 84 citations.

Table 2 shows the distribution for the uses of these 15 main essential oils found in this search, amongst the nine main sub-groups of the IPC listed in previous Figure 2. The last column showed in Table 2 indicates the percentage of participation of each essential oil face the total of 1,564 joined citations. The last line designates the joint participation of 94.31% for these same essential oils.

About terpenics/terpenoids compounds

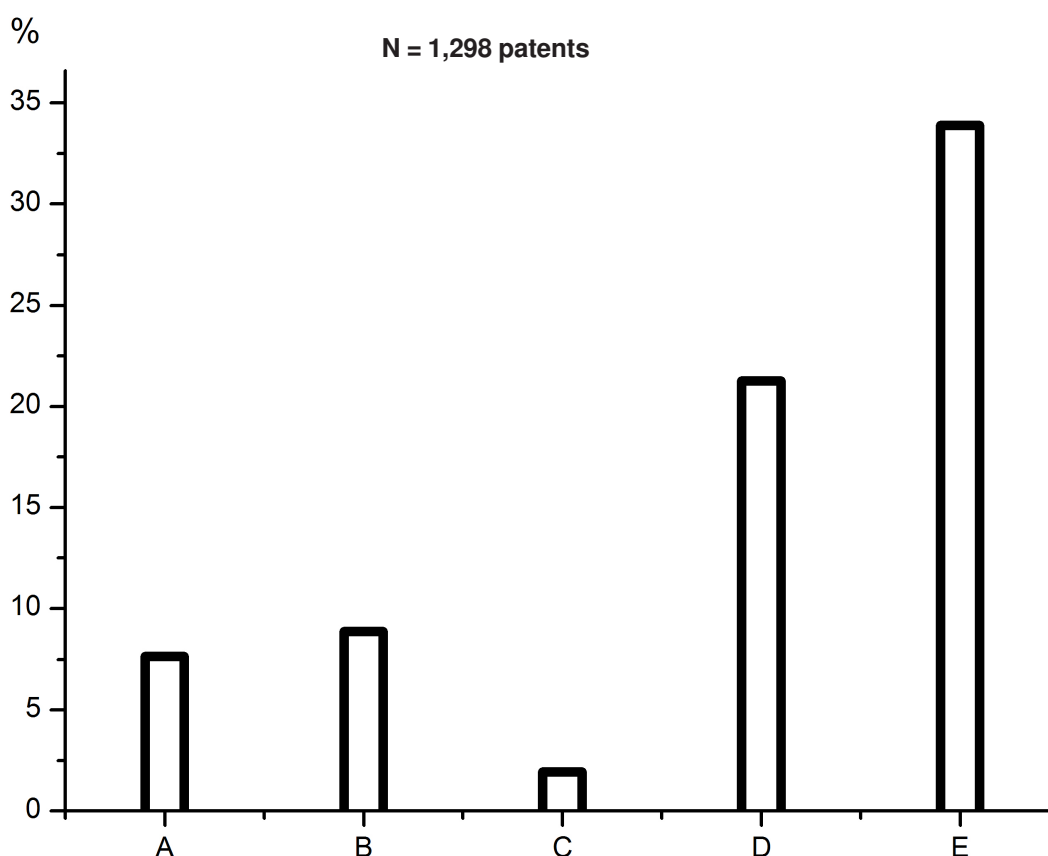


FIGURE 2. Groups and Subgroups from IPC applied in USPTO granted patents for the use of essential oils, terpenics/terpenoids compounds in the pharmaceutical sector between 1980-2003. (A) A61K 47/46 - Medicinal preparations containing Ingredients of undetermined constitution or reaction products thereof characterized by their non-active ingredients; (B) A61K 6/02 - preparations for dentistry for artificial teeth, for filling or for capping teeth; (C) A61K 9/20 - Medicinal preparations characterized by special physical form like Pills, lozenges or tablets; (D) A61K 35/78 - Medicinal preparations containing Materials from plants or reaction products thereof with undetermined constitution; (E) A61K 31/33 - Medicinal preparations containing Heterocyclic compounds like organic active ingredients.

(Table 3), 15 had answered for 97.14% of 1,069 citations, like limonene (extracted from citrus essential oils; 88 citations), camphor (extracted from camphor essential oil; 192 citations), menthol (extracted from mints essential oils; 305 citations) and pinene (extracted from essential oils of the species pine or eucalyptus; 41 citations).

Table 3 shows the distribution for the uses of these 15 main terpenics/terpenoids compounds, amongst the nine main sub-groups of the IPC listed in previous Figure 2. The last column in Table 3 indicates the percentage of participation of each compound face the total of 1,069 joined citations. The last line designates the joint participation of 97.14% for these same substances.

The 1,298 patents belongs to following groups of owners: a) 455 companies answering by

700 documents (or 53.93%); b) 46 researches centers (governmental agencies, universities, institutes and foundations) with 388 patents (29.89%); and c) 168 Individually Owned Patent (IOP) with 210 patents (16.18%). The most owners were geoeconomically distributed by United States (44.61%), Japan (12.40%) and Germany (5.24%). Others nationalities (that had added 37.75%) were Argentine, Australia, Belgium, Canada, China, Colombia, Denmark, France, Great Britain, Greece, India, Ireland, Israel, Italy, Mexico, Netherlands, Portugal, South Korea, Spain, Sweden, Switzerland, Taiwan and Uruguay.

About Individually Owned Patent (IOP), North Americans answered by 70.48% of the 210 found patents, Japanese with 6.01% and French by 5.23% (others nationalities had added 18.28%,

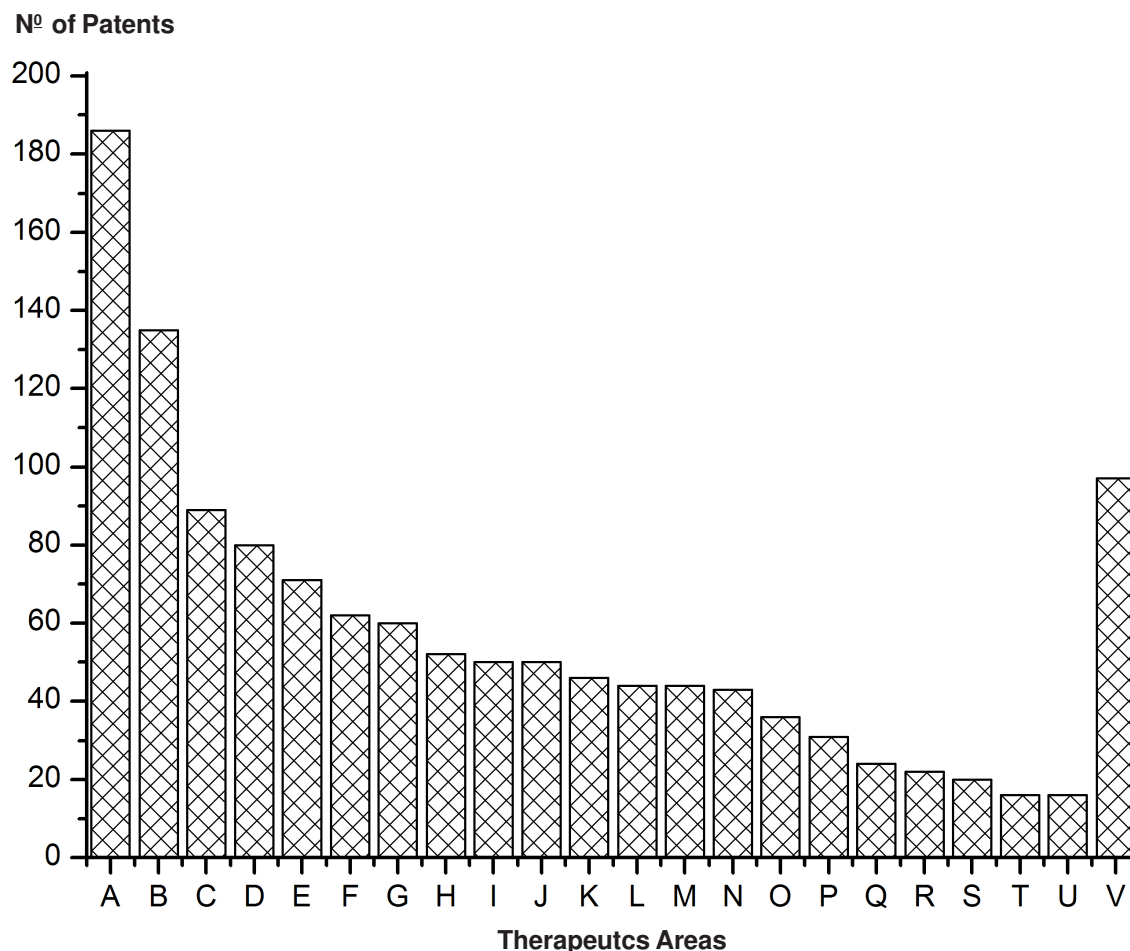


FIGURE 3. Therapeutics areas described in the USPTO granted patents for the use of essential oils, terpenics/terpenoids compounds in the pharmaceutical sector between 1980-2003. A: Dermatological compositions; B: Antibiotic compositions; C: Analgesic compositions; D: Nutritional compositions; E: Antiinflammatories compositions; F: Neurological compositions; G: Gastrointestinal compositions; H: Delivery System compositions; I: Adjuvant compositions; J: Pharmaceutical tablets; K: Flavor compositions; L: Expectorant compositions; M: Heart diseases treatment compositions; N: Anticancer compositions; O: Dental compositions; P: Osseous tissue compositions; Q: Dietetical Compositions; R: Cholesterol Reducer compositions; S: Inductor to Cellular immunological response; T: Antioxidant compositions; U: Ophtalmic compositions; V: Others (anaesthetic compositions; hair loss treatment; procreation compositions; estabilizant compositions; enzyme inhibitors compositions; antidiabetic compositions; antiallergic compositions; injectable formulations; erectile dysfunction treatment compositions; incontinence treatment compositions; antitussive compositions; dysmenorrhea treatment compositions and endometriosis treatment compositions).

see list above). The ratio between the total number of IOPs listed and the total number of patents that pertaining to IOPs was equal to 1:1.25. Table 4 list the researches centers and its countries.

Also in companies, the ratio between the total number of companies and the total number of patents was low, equal to 1:1.54. Figure 4 shows the top 20 companies with an average ratio up than 10 patents/firm. Amongst them, besides the 5 from top 10 pharmaceutical global firms (Pfizer (US), GlaxoSmithKline (UK), Merck (US), Bristol-Myers

Squibb (US) e Aventis Pharma Group (FR/DE)) [14], there are leader companies in the food, cosmetics and personal care segments: L'Oreal (France; cosmetic and cosmeceutic), Procter & Gamble (US; personal care), Monsanto (US; nourishing biotechnology) and Kimberly-Clark (US; personal care).

CONCLUSION

This study identified 1,298 granted patents from United States Patent and Trademarks Office

TABLE 2. Most Important Essential Oils by Subgroups of A61K Subclass from IPC

Essential Oils Subgroups from A61K										
	A61K 31/33	A61K 35/78	A61K 6/02	A61K 9/10	A61K 9/14	A61K 9/20	A61K31/1 85	A61K 31/70	A61K 47/46	%
Sesame	14.90	1.73	0.90	1.02	1.41	2.56	3.20	1.15	1.09	27.94
Orange	1.60	2.30	0.83	0.13	1.28	1.53	1.21	0.83	0.96	10.68
Peppermint	1.15	2.24	0.83	0.38	1.02	1.53	2.11	0.45	0.51	10.23
Lemon	0.70	2.69	0.51	0.19	0.64	2.62	1.15	1.09	0.77	10.36
Pine	4.28	1.53	0.58	0.00	0.19	0.38	0.38	0.32	0.58	8.25
Eucalyptus	0.19	1.53	0.26	0.45	0.45	0.58	0.51	0.26	0.45	4.67
Spearmint	0.19	0.58	0.64	0.00	0.19	0.19	1.21	0.26	0.19	3.45
Clove	0.19	1.15	0.38	0.19	0.38	0.26	0.70	0.19	0.19	3.64
Ginger	0.06	1.47	0.26	0.00	0.45	0.13	0.38	0.00	0.13	2.88
Rosemary	0.13	1.21	0.32	0.06	0.26	0.32	0.38	0.06	0.19	2.94
Pepper	0.00	1.21	0.32	0.06	0.26	0.32	0.38	0.06	0.19	2.81
Rose	0.06	0.70	0.45	0.38	0.06	0.38	0.26	0.13	0.00	2.43
Grapefruit	0.26	1.15	0.19	0.00	0.06	0.06	0.19	0.19	0.00	2.11
Bergamot	0.06	0.38	0.19	0.06	0.06	0.06	0.06	0.00	0.00	0.90
Garlic	0.19	0.51	0.06	0.00	0.06	0.06	0.00	0.06	0.06	1.02
										94.31

A61K 31/33 - Medicinal preparations containing Heterocyclic compounds like organic active ingredients; A61K 35/78 - Medicinal preparations containing Materials from plants or reaction products thereof with undetermined constitution; A61K 6/02 - preparations for dentistry for artificial teeth, for filling or for capping teeth; A61K 9/10 - Medicinal preparations characterized by special physical form like Dispersions or Emulsions; A61K 9/14 - Medicinal preparations characterized by special physical form like Particulate Material; A61K 9/20 - Medicinal preparations characterized by special physical form like Pills, lozenges or tablets; A61K 31/185 - Medicinal preparations containing Acids, Anhydrides, halides or salts thereof like organic active ingredients; A61K 31/70 Medicinal preparations containing Carbohydrates, Sugars, Derivatives thereof like organic active ingredients; A61K 47/46 - Medicinal preparations containing Ingredients of undetermined constitution or reaction products thereof characterized por serem non-active ingredients.

TABLE 3. Most Important Terpenes and Terpenoids Compounds by Subgroups of Subclass A61K from IPC

Terpenes and Terpenoids Compounds Subgroups from A61K										
	A61K 31/33	A61K 35/78	A61K 6/02	A61K 9/10	A61K 9/14	A61K 9/20	A61K 31/185	A61K 31/70	A61K 47/46	%
Menthol	5.22	5.09	2.29	3.56	1.91	4.07	4.20	1.53	1.15	29.03
Squalene	8.02	0.51	1.27	2.55	0.64	1.15	1.02	1.53	0.64	17.31
Camphor	6.37	3.44	2.55	4.20	1.15	1.02	1.40	1.53	1.53	23.17
Limonene	1.66	1.27	0.38	0.51	0.89	0.13	0.38	0.38	0.13	5.73
Pinene	0.64	1.27	0.13	0.00	0.13	0.13	0.13	0.00	0.00	2.42
Thymol	0.38	1.15	0.76	0.13	0.00	0.38	0.64	0.00	0.00	3.44
Eucalyptol	0.51	0.51	0.51	0.00	0.38	0.64	0.64	0.13	0.00	3.31
Retinol	1.27	0.38	0.25	0.76	0.38	0.00	0.00	0.64	0.25	3.95
Geraniol	0.13	0.25	0.38	0.25	0.25	0.25	0.00	0.13	0.00	1.66
Pentadiene	0.13	0.00	0.13	0.51	0.25	0.00	0.25	0.13	0.00	1.40
Linalool	0.13	0.64	0.25	0.00	0.13	0.13	0.00	0.00	0.00	1.27
Citral	0.00	0.13	0.00	0.25	0.13	0.13	0.00	0.00	0.13	0.76
Menthane	0.13	0.25	0.25	0.00	0.13	0.00	0.51	0.38	0.00	1.66
Carvone	0.00	0.51	0.00	0.00	0.25	0.00	0.64	0.00	0.00	1.40
Camphene	0.25	0.25	0.00	0.00	0.13	0.00	0.00	0.00	0.00	0.64
										97.14

A61K 31/33 - medicinal preparations containing Heterocyclic compounds like organic active ingredients; A61K 35/78 - medicinal preparations containing Materials from plants or reaction products thereof with undetermined constitution; A61K 6/02 - preparations for dentistry for artificial teeth, for filling or for capping teeth; A61K 9/10 - Medicinal preparations characterized by special physical form like Dispersions or Emulsions; A61K 9/14 - Medicinal preparations characterized by special physical form like Particulate Material; A61K 9/20 - Medicinal preparations characterized by special physical form like Pills, lozenges or tablets; A61K 31/185 - Medicinal preparations containing Acids, Anhydrides, halides or salts thereof like organic active ingredients; A61K 31/70 Medicinal preparations containing Carbohydrates, Sugars, Derivatives thereof like organic active ingredients; A61K 47/46 - Medicinal preparations containing Ingredients of undetermined constitution or reaction products thereof characterized por serem non-active ingredients.

Nº of Patents

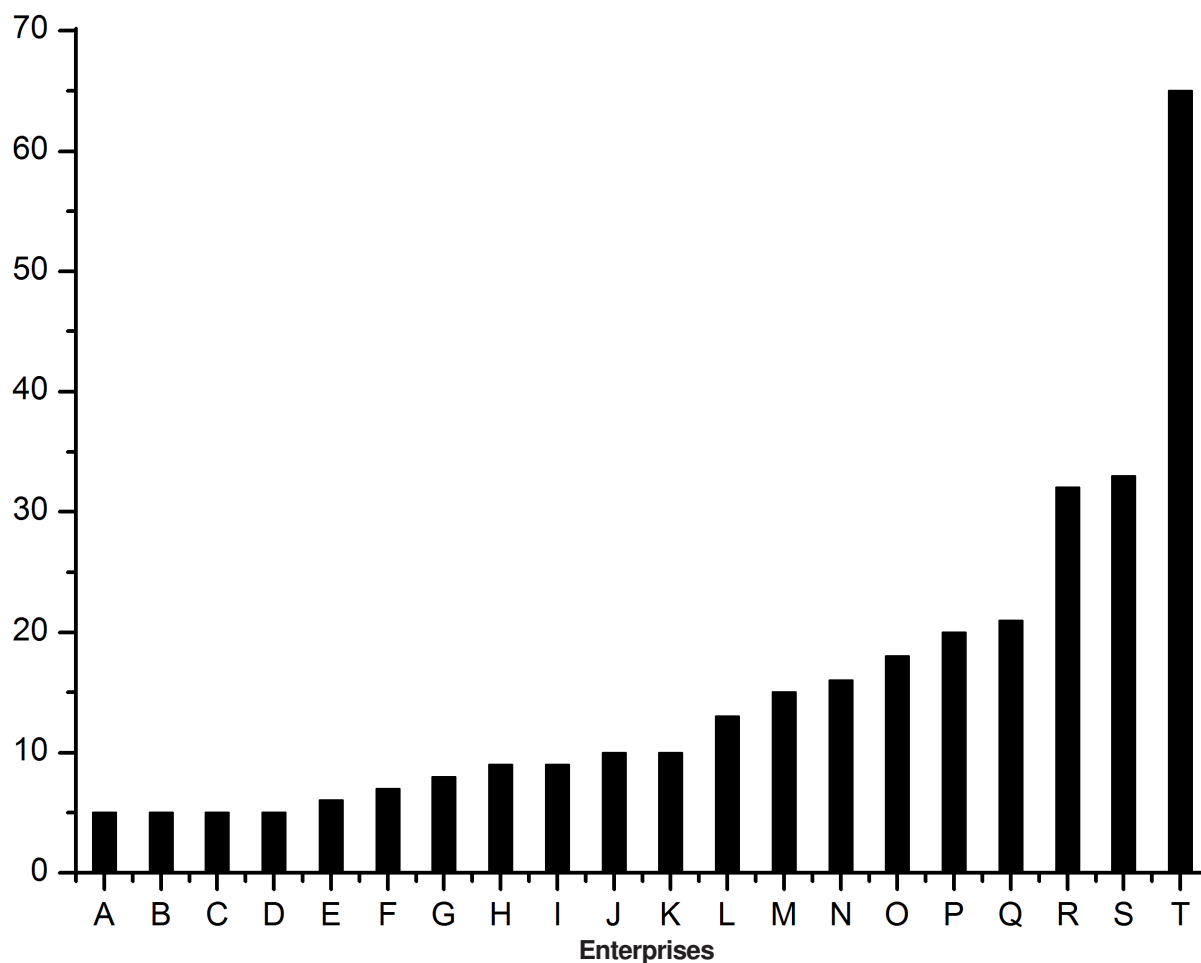


FIGURE 4. Top 20 USPTO granted patents owners companies related with the use of essential oils, terpenics/terpenoids compounds in the pharmaceutical sector between 1980-2003. A - Univ.Texas System (US); B - Conopco (US); C - Bayer (DE); D - Beth Israel Deaconeses Medical Centre (US); E - US Health Dept. (US); F - KAO Corp. (JP); G - Takeda Co. (JP); H - Kimberly-Clark (US); I - Monsanto (US); J - American Home Products (US); K - Council of Scientific and Ind. Research (IN); L - Scherinhg-Plough (US); M - Abbott (US); N - Merck (DE); O - Bristol-Myers-Squibb (US); P - Pfizer (US); Q - GlaxoSmithKline (GB); R - Procter & Gamble (US); S - L'Oreal (FR); T - Aventis Pharma Group. Country codes: DE – Germany; FR – France; GB – Great Britain; IN - India; JP – Japan; US – United States of America. Aventis Pharma Group is a French-German company formed in 1999, after merger of French Rhône-Poulenc and German Hoechst Marion Roussel (HMR) – the pharmaceuticals division of the German Hoechst AG.

related with the use of essential oils, terpenics/terpenoids compounds in the pharmaceutical sector between 1980-2003. The major therapeutics uses were in the dermatological, antibiotic, analgesic, anti-inflammatory, neurological, gastrointestinal, heart diseases and anticancer areas. Among the essential oils, three groups were the most cited: citrus, mints and condimentous; and among terpenics/

terpenoids compounds: menthol and limonene. Besides the expected list of pharmaceutical companies, can be found three cosmetic and personal care firms: L'oreal, Procter & Gamble and Kimberly Clark. From the most important therapeutic classes, six were rolled in this research: Heart diseases, Central Nervous System, Alimentary/Metabolism, Anti-infectious, Breathing, Skeleton/Muscle.

TABLE 4. List of Universities and Researches Centers

Beth Israel Deaconeses Medical Centre (US)	University of Gent (BE)
Cancer Res. Found. of Contra Costa (US)	University of Iowa (US)
Cedars Sinai Medical Center (US)	University of Jerusalem (IL)
Chemo-Sero-Therapeutic Inst. (JP)	University of Kansas State (US)
Commonwealth Scientific and Ind. Res. Org. (AU)	University of Max-Planck (DE)
Council of Scientific and Industrial Res. (IN)	University of Medical and Dental Schools of Guy's (US)
Harbor Branch Oceanographic Inst. (US)	University of Medicine and Dentistry of New Jersey (US)
Illinois Inst. of Techn. (US)	University of Memphis (US)
Int'l Nutrition Res. Institute (SE)	University of Michigan (US)
Kitasato Inst. (JP)	University of Mississippi (US)
Korea Res. Inst. of Chemical Techn. (KR)	University of Missouri (US)
Longevity Inst. Int'l (US)	University of Montreal (CA)
Massachusets Inst. of Techn. (US)	University of of Patents (US)
Mount Sinai School of Medicine (US)	University of of Pharmaceutical Sciences (IN)
National Science Council (TW)	University of Queens (CA)
New Mexico Tech. Res. Foundation (US)	University of Ramot (IL)
Oklahoma Medical Res. Foundation (US)	University of South Florida (US)
Shriners Hospital for Crippled Children (US)	University of St. Louis (US)
The Scripps Res. Inst. (US)	University of Texas System (US)
University della Ricerca Scientifica e tecnologica (IT)	University of Traditional Chinese Medicine Res. (JP)
University of Arkansas (US)	University of Washington State (US)
University of Bar-Ilan (IL)	
University of California (US)	

REFERENCE

ARAÚJO, V.M.R.H. Uso da informação contida em patentes nos países em desenvolvimento. **Ciência da Informação**, v.13, n.1, p.53-6, 1984.

ARCHIBUGI, D.; MICHIE, J. The globalisation of technology: a new taxonomy. **Cambridge Journal of Economics**, v.19, n.1, p.121-40, 1995.

CRAVEIRO, A.A.; QUEIROZ, D.C. Óleos essenciais e química fina. **Química Nova**, v.16, n.3, p.224-8, 1993.

JOULAIN, D. Investgating new essential oils: rationale, results and limitations. **Perfumer & Flavorist**, v.18, n.5, p.3, 1993.

LOZANO, R.S. Indicadores de los sistemas de ciencia, tecnología e innovación. **Economía Industrial**, n.343, p.97-109, 2002.

MONTANARI, C.A.; BOLZANI, V.S. Planejamento racional de fármacos baseado em produtos naturais. **Química Nova**, v.24, n.1, p.105-11, 2001.

NEWMAN, D.J.; CRAGG, G.M.; SNADER, K.M. Natural products as sources of new drugs over the periodo 1981-2002. **Journal of Natural Products**, v.66, n.7, p.1022-37, 2003. Disponível em: <<http://pubs.acs.org/cgi-bin/>

sample.cgi/jnprdf/2003/66/i07/pdf/np0300961.pdf>. Acesso em: 05 fev. 2004.

REINBOTHE, C.; DIETRICH, B.; LUCKNER, M.J. Regeneration of plants from somatic embryos of digitalis-lanata. **Journal of Plant Physiology**, v.137, p.224, 1990.

SEIDL, P.R. Pharmaceuticals from natural products: current trends. **Anais da Academia Brasileira de Ciências**, v.74, n.1, p.145-50, 2002.

SILVA-SANTOS, A.; ANTUNES, A.M.S.; D'AVILA, L.A. New natural linalool sources: research and industrial application. **Perfumer & Flavorist**, v.29, n.3, p.38-43, 2004.

UNITED STATES PATENT AND TRADEMARKS OFFICE (USPTO). **Databank**. Disponível em: <<http://www.uspto.gov>>. Acesso em : 03 jan. 2002 - 15 mar. 2004.

WILSON, R.M. Patent analysis using on line databases: technological trend analysis. **World Patent Information**, v.9, n.1, p.18-26, 1987.

WORLD INTELLECTUAL PROPERTY ORGANIZATION (WIPO) - **International Patent Classification**. Disponível em: <<http://www.wipo.int/classifications/en>>. Acesso em: 07 jan.2002 - 15 abr. 2004.