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Progress in the study of chemical composition and biological function of rosemary

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Abstract: *Rosemary is a kind of labiatric plant with rich value. Its main chemical components include flavonoids, terpenoids, organic acids and amino acids. On this basis, the biological effects of antibacterial, anti-oxidation, anti-inflammatory, anti-tumor, anti hyperglycemia and nerve injury were studied. The results provide scientific basis for further research of rosemary.*

Keywords: *Rosemary; Oxidation resistance; Biological action; Application*

1. Introduction

Rosemary, also known as oil and weed, is also known as the sea dew, chrysanthemum, etc[1] , is Dicotyledona, Labiatae, RosemaryBotany.It is originated from Europe, North Africa and Mediterranean coast, mainly distributed in France, Spain, Yugoslavia, Tunisia, Morocco, Bulgaria and Italy, and is now widely planted in various countries around the world[2]. According to the literature, the first three kingdoms introduced the Central Plains from the western region, and was widely planted in the source of Shaying River (Yuzhou, Xuchang).In 1981, the Institute of Chinese Academy of Sciences introduced the seed test successfully from the United States as a spice crop. At present, the main planting areas in China are Guangxi, Guizhou, Yunnan, Hainan, Xinjiang and Beijing[3.4]. Nowadays, many researchers have done a lot of research on the chemical components and biological functions of rosemary, but the summary of the classification and biological effects of rosemary is not comprehensive. This paper introduces the extraction technology of rosemary, and summarizes its chemical components and biological functions, hoping to provide scientific basis for the exploitation of rosemary resource value.

2. Extraction process of rosemary

2.1. Water vapor distillation extraction method

The water vapor distillation method is mainly used to extract the volatile components of rosemary, based on the principle of Dalton's law , due to the difference in vapor pressure of each component of the volatile oil, the essential oil is extracted from the raw material using water vapor[5] . The factors affecting the extraction process by hydro-distillation are mainly the crushing degree of the herb, the soaking time of the herb, the amount of water added, and the extraction time. Zhang Junqing et al. (2011) used hydrodistillation to extract the volatile oil of rosemary and obtained a purer volatile oil by heating reflux[6] . The hydrodistillation method can also be used in concert with other methods of extraction, such as salinization-water vapor distillation, ultrasound-assisted hydrodistillation, and microwave shock-assisted hydrodistillation extraction, to improve the extraction rate and reduce the extraction time of rosemary[7] . The advantages of water distillation method are simple operation, lower cost, and can reduce the distillation temperature of spice components to prevent the decomposition or deterioration of the extract, the extraction process is more mature, the yield is large, and no pollution to the environment. But the water distillation method of extraction process is longer, the system is open, the process will cause thermal instability and easy to oxidize the loss of components, some components have a destructive effect, so only for the extraction of essential oils. In recent years, molecular distillation has also been used to extract the volatile oil of rosemary, and the types of volatile oil components extracted are basically the same as those extracted by water distillation, and have the advantages of low temperature, high efficiency of heat transfer, short heating time and higher degree of separation, but the requirements for equipment are relatively high and do not facilitate industrial development.

2.2. Solvent extraction method

Solvent method is the extraction of rosemary in the effective substances commonly used extraction method, the method is the use of organic solvents such as petroleum ether, hexane, ethyl acetate, acetone, ethanol as the extraction solvent[8, 9] , taking into account the safety, effective, economic and other factors, rosemary extraction generally used ethanol as the organic solvent, ethanol is suitable for extraction in 2 h, the liquid to material ratio of 10:1[10] . The concentration of ethanol should not be too large, so as not to dissolve the non-polar substances in rosemary also, such as chlorophyll. And the method is often combined with microwave shaking and other methods to achieve higher yields. Wang Y et al. (2012) showed that the parameters affecting the yield of rosemary antioxidants and its total phenolic acid content are mainly ethanol concentration, extraction temperature, material-to-liquid ratio, extraction time and number of extractions[11] . Extraction with solvents is generally performed by reflux extraction, soxhlet extraction, percolation extraction, and cold soak extraction.[12] . Cold soak and percolation extraction are suitable for heat-sensitive components, but more time-consuming; while reflux extraction and Soxhlet extraction are relatively short and efficient. The solvent method was more efficient for the extraction of rosemary antioxidants with higher yield of flavonoids[13] . Han Yuanyuan et al. (2012) analyzed the extraction of herbs rich in syringic acid by solvent method, which has high extraction rate and good stability and is suitable for industrial application[14] . Liang Z.Y. et al. (2010) extracted ursolic acid from rosemary by solvent method, the extraction rate was 92.38% with high purity, and a variety of antioxidant components in rosemary could be extracted at the same time[15] . This method has the advantages of being safe, effective, environmentally friendly, easy to operate, and relatively low cost[16] . However, the disadvantage of the solvent method is that syringic acid is greatly affected by the operating conditions during the separation process, and it is easily converted into oxidation intermediate product syringol, which reduces the antioxidant effect and makes the product difficult to meet the international market requirements.

2.3. Ultrasonic extraction method

With the emergence of a variety of specialized industrial extraction equipment such as ultrasonic cycle-enhanced extraction and continuous countercurrent ultrasonic extraction, ultrasonic extraction of the active ingredients of plants has become a reality[17] . Rosmarinic acid, syringic acid, syringol, ursolic acid, oleanolic acid, etc. can be extracted from rosemary mainly by ultrasonic extraction[18] . The yield of syringic acid and rosmarinic acid gradually increased with the increase of time during the extraction process, and the yield of syringic acid tended to decrease after 50 min, presumably due to partial degradation or isomerization of syringic acid under the effect of prolonged sonication. The effect of feed-to-liquid ratio on the yield of rosmarinic acid was not significant, but the effect on the yield of syringic acid was significant. Ultrasonic cycle was an effective method for the extraction of syringic acid and rosmarinic acid from rosemary. Bi Liangwu et al. (2007) used a bath trial ultrasonic generator and a probe extraction method generator to extract antioxidants from rosemary, and the yields of antioxidants extracted at room temperature for 10 min and 30 min were 13.4% and 12.8%, respectively.[19] . Paniwnyk et al. (2009) showed that rosmarinic acid, syringic acid, and other antioxidant components were extracted from rosemary by ultrasound method, respectively. (2009) showed that the extraction of rosmarinic acid, syringic acid, and other antioxidant components from rosemary by ultrasonication, respectively, and indicated that the extraction of syringic acid was more favorable with dried leaves or water-free solvent, and the extraction solvent ethanol was superior to methanol[20] . Although the extraction time of ultrasonic extraction is long, but the liquid impurities are few, the active ingredients are easy to be separated and purified; the extraction temperature is low, the active ingredients are not easy to be spoiled; the operation cost of extraction process is low, the comprehensive economic benefits are significant; the operation is simple and easy, the equipment maintenance, maintenance is convenient, etc.[21]

2.4. Supercritical carbon dioxide extraction method

One-step extraction of active ingredients of rosemary by supercritical carbon dioxide extraction technique is a hot research topic in recent years. The method is mainly used to extract essential oil and antioxidants (rosmarinic acid, syringic acid, etc.). Le Zhenjang et al. (2009) used supercritical carbon dioxide extraction to extract the antioxidant components of natural rosemary. The optimal extraction parameters were 40 MPa, 80 ℃, 20% water addition, and 2.5 h access time. rosmarinic acid, syringic acid and other components were mainly extracted[22] . Supercritical carbon dioxide extraction technique can obtain rosemary essential oil and antioxidants in one step, the method is simple, fast and efficient,

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and the resulting essential oil is pure in quality and high in antioxidant active ingredients[23] . This method has been widely used in the extraction and isolation of natural antioxidants due to its low cost, non-pollution, energy saving, easy operation, environmental protection, and the advantages of simultaneous separation and purification[24] . However, supercritical CO2 extraction is limited by the processing capacity and low yield, which makes industrial development difficult at present.

2.5. Subcritical fluid extraction method

Subcritical fluid extraction is a very promising technique for extracting solid samples, whose main fluids are liquefied butane and propane, and more enthusiastically water as a fluid in recent years. It is the use of subcritical fluid as an extractant, in a low-pressure, oxygen-free, closed vessel, according to the principle of similar compatibility, through the process of molecular diffusion between the extracted material and the extractant in the process of immersion bubbles, the product is separated from the extractant by evaporation under reduced pressure. This technique is significantly characterized by easy control of the mesoelectricity and is widely used abroad, and recently the extraction of essential oils and antioxidant components from plants (rosemary, etc.) has also been reported in China. Eddie Chen et al. (2009) used subcritical water extraction to study the extraction of a variety of herbal medicines, in which flavonoids, saponins, terpenoids, antioxidants and volatile oils were extracted from rosemary. The main parameters affecting the extraction include temperature, time, organic solvent, addition of surfactants, and number of extractions[25] . Compared with other extraction methods, subcritical fluid extraction not only overcomes the shortcomings of other methods, but also retains the advantages of supercritical extraction, a large selection of solvents, a wide range of fluid sources, reduced price, low solubility consumption, high extraction quality, environmental protection, rapid, suitable for heat-sensitive components, etc., and has broad application prospects.

2.6. Microwave extraction method

Microwave-enhanced extraction has been used in many herbal medicine extraction lines in China, mainly for extracting the oil and alkaloid components of rosemary. Microwave has different effects on different parts of the plant and different tissues, and the release of intracellular products is selective, so different treatment methods should be used according to the characteristics of plant products and their different parts. Wang Naixin (2011) used microwave-assisted extraction of rosemary volatile oil, the best process conditions: the material-to-liquid ratio of 12.3 mL /g, extraction time of 125 s, microwave power of 500 W, extraction rate of 4.05%[26] . The microwave method can penetrate the extraction medium and heat it directly, which can shorten the extraction time and improve the extraction efficiency. Microwave extraction is less limited by the affinity of the solvent, more solvents are available, while reducing the amount of solvent. In addition, microwave extraction if used for large-scale production, it is safe, reliable, non-polluting, green engineering, the composition of the production line is simple, and can save investment. In general, microwave extraction without drying and other pretreatment, simplifying the process, reducing investment, and the results of the extraction is not affected by the water content of the substance, can be recovered, with the advantages of strong selectivity, short operating time, less solvent consumption, easy to control, simple equipment, environmental protection, low investment, etc.

2.7. Other extraction methods

Other extraction methods used to extract the active ingredients of rosemary include enzymatic hydrolysis, microencapsulation double aqueous phase extraction, etc. Enzymatic extraction of essential oil is a new type of extraction method, which is based on the composition of plant cell wall, using the highly specific characteristics of enzymes to select the corresponding enzymes to hydrolyze and degrade the components of the cell wall and destroy the cell wall structure, so that the intracellular active ingredients dissolve, miscible or colloidal into the solution, thus achieving the purpose of extraction. This method can shorten the extraction time and high purity of active ingredients, but the technical requirements are high. Microencapsulation double aqueous phase extraction method is the combination of microencapsulation and double aqueous phase technology used, which not only improves the extraction efficiency and purification of volatile oils, but also effectively protects the transformation of unstable components during the extraction process.

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3. The chemical composition of rosemary

Rosemary includes flavonoids, terpenoids, organic acids, amino acids and other chemical components, some of which are classified as shown in the structural formula in Figure 1:

3.1. Flavonoids

The flavonoids in the dried leaves of rosemary were extracted by organic solvent method, and the flavonoid content of the extracts was determined by UV spectrophotometry. The optimized process was as follows: extraction temperature 80°C, ethanol concentration (v/v) 50%, extraction time 2h, material-liquid ratio 1:11 g/m L, particle size 60~80 mesh. Under the optimized process, the total flavonoid dry basis yield was 8.23%, and the total flavonoid content in the extracts reached 24.44%[27] .

More than twenty flavonoids were isolated and identified from its stems and leaves. They mainly include 6-methoxy lignan, hesperidin (Hesperidin), isohesperidin, Diosimin, Homoplantagin, Heptyl indican, 6-methoxy lignan, 6-hydroxy lignan -7-glucose glucoside, 3,5,7-trihydroxyflavone, 8-methoxycannabinoid, apigenin, luteolin, genkwanin, diosmetin, hispidulin, chrysin, galangin, quercetin. Quercetin kaempferol , 5-hydroxy-7,4-dimethoxyflavone, 5,4-dihydroxy-7-methoxyflavone, cuneolin-3-O-glucoside , cuneolin-4-O-glucoside, lignan-3-O-glucuronide, corianderin-7-methyl ether, 6-methoxy-3,4-dihydroxyflavone-7-O- glucoside, lignan-7-glucoside, etc.

3.2. Terpenoids

Terpenes are an important class of metabolites in natural products with a five-carbon basic unit of isoprene in the molecule with the general formula (C5 H8)n. The largest number of terpene components isolated and identified from rosemary to date include monoterpenes, sesquiterpenes, diterpenes and triterpenes.

3.2.1. Monoterpenes and sesquiterpenoids

These two terpene components are complex and are mainly present in the essential oil of rosemary and petroleum ether extracted fraction. They were extracted mainly by hydrodistillation and supercritical extraction wind method, and identified mainly by GC-MS.[28] . The main monoterpene and sesquiterpene components in rosemary are α-pinene, camphene, T-pinene, β-pinene, U-pinene, α-caryophyllene, 1,8-cineole (1,8-cineole), Bornyl acetate, α-phellandrene, α-terpinene, α-terpineol, β-caryophyllene, Camphor, Borneol Linalool, p-cymene, Limonene[29] .

3.2.2. Second post class

The diterpenoid skeleton in rosemary is mainly rosmarinic acid, which can be divided into diterpenoid phenolics and diterpenoid quinones, the main biologically active class of compounds in rosemary. The diterpene phenolic compounds include carnosic acid, carnosol, rosemary phenol, rosemary methyl ester, 7-methoxyrosmanol, 7-ethoxyrosmanol, epirosmanol, epirosmanol, epirosmanol, epirosmanol. epirosmanol), isorosmanol (Isorosmanol)

Rosmarinic acid, rosemary dialdehyde (Rosmaridial), rosemary diphenol (R0smaridiphenol), rosmarinicine, iso-rosmarinicine, 7-isopropoxy-epi-rosmarinol (7-O-iso-propyl-epirosmanol), and Ferruginol (Ferruginol), etc. The one with the largest proportion of content is fat-soluble syringic acid. The main components of diterpene quinones are epitantanone (Cryptotanshinone), rosemariquinone, rosemarinone, 7-isopropoxy-rosemaryquinone (7-O-isopropyl rosmaquinone), larch dioquinone (Taxadione), and Horminone, 7-α-acetoxy-roylearlone, 7-α-hydroxy-royleanone, etc.[30]

3.2.3. Triterpenoids and sterols

Most of the triterpenoids isolated from rosemary plants are triterpenic acids, with the parent nuclei being ursolic, oleanolic and lupine. They mainly include: Ursolic acid, oleanolic acid, Betulinic acid, 19-α-hydroxyursolic acid, 2β-hydroxy oleanolic acid, 3β-hydroxyursolide-12,20(30)-diene- 17-oic acid, 3-O-acetyl oleanolic acid, 3-Ü-acetyl ursolic acid, and 3-O-acetyl ursolic acid. Sterols include Betulinol, Taraxerol, α-,β-Amyrin, lupinol, lupulinol, geraniol, cholestrol, rape oil sterol, glutathione, α-betulinone, β-betulinone, epi-α-Amyrin[31] .

3.3. Organic acids

The organic acids in rosemary are mainly hydroxycinnamic acid: p-coumaric acid (p-Coumaric

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acid), chlorogenic acid (Chlorogenic acid), rosmarinic acid (rosmarinic acid), ferulic acid (Ferulic acid), m-hydroxybenzoic acid, coumaroylquinic acid, coumaric acid, etc.; hydroxybenzoic acid: coumaric acid (vanillic acid), syringic acid (Syringate), caffeic acid (Caffeic acid), proto-catechuic acid (Protocatechuic acid), dicaffeic quinic acid; hydroxyphenylacetic acid: homovanillic acid (Homovanillic acid) and p-hydroxybenzoic acid[32] .

3.4. Amino acids

Wu (2006) found that 17 amino acids were detected in rosemary by AccQ-Tag method, namely: Aspartic acid (Asp), Serine (Ser), Glutamic acid (Glu), Glycine (Gly), Arginine (Arg), Histidine (His), Threonine (Thr), Tyrosine (Tyr), Pro Valine (Val), Leucine (Leu), Isoleucine (Ile), Cysteine (Cys2), Alanine (Ala), Methionine (Met), Phenylalanine (Phe), Lysine (Lys), of which 8 are essential amino acids[33] .

3.5. Other categories

The fatty acids isolated from rosemary leaves mainly include 6,7,16-trihydroxydecanoic acid, 10,16-dihydroxyhexadecanoic acid, and 9,10,18-trihydroxyoctadecanoic acid. Rosemary leaves also contain 97% alkanes, 2.3% aliphatic cyclic olefins, including 84% n-alkanes and 16% branched alkanes in saturated aliphatic hydrocarbons[34] .

4. Classification of rosemary extract

The analytical determination methods of rosemary extract mainly include: meteorological chromatography, high performance liquid chromatography, mass spectrometry, ultraviolet spectrometry, micellar electrokinetic chromatography, infrared spectrometry, capillary electrophoresis, nuclear magnetic resonance spectrometry, etc. The most used analytical method is high performance liquid chromatography.

4.1. Water-soluble extracts

The water-soluble extracts mainly include rosmarinic acid, ferulic acid, caffeic acid, chlorogenic acid, L-acsorbic acid, hesperidin and isohesperidin. (isohesperidin), etc.[35] . Currently, the most studied ones include the following: rosmarinic acid, molecular formula C18 H O168 , molecular mass 360.31; caffeic acid, molecular formula C H98 O4 , molecular mass 180.16; ascorbic acid, i.e. vitamin C, molecular formula C6 H8 O6 , molecular mass 176.12.

4.2. Fat-soluble extracts

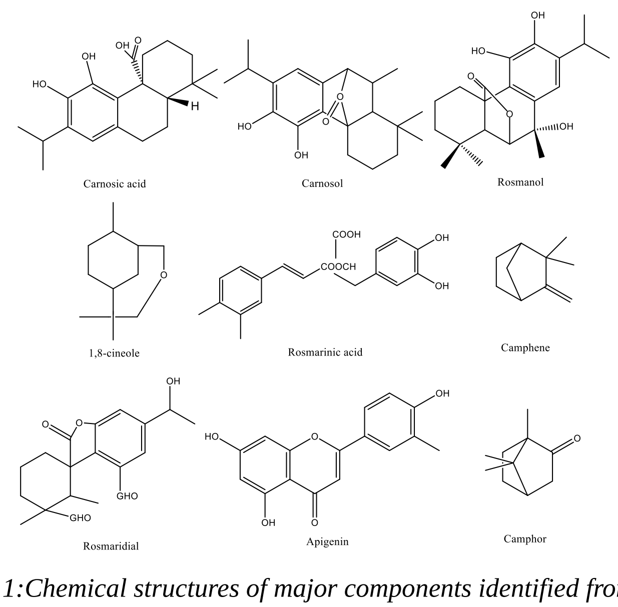

Figure 1:Chemical structures of major components identified from rosemary

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Fat soluble extracts include Carnosic acid, Carnosol (Carnosol), Rosmanol, 7-methoxyrosmanol, 7-ethoxyrosmanol, oleanolic acid, naringenin, sesquiterpene, ursolic acid, rosmarinic acid, isorosmarinic acid, etc. At present, the most studied ones mainly include syringic acid, syringol, ursolic acid and oleanolic acid[36] . Among them, ursolic acid and oleanolic acid are mutual triterpenoid isomers with similar properties and can exist simultaneously, while syringic acid can be converted into methyl syringylate and syringol, and syringol can be converted into rosmarinic acid, epi-rosmarinic acid and 7-methoxy rosmarinic acid.

5. Biological functions of rosemary

5.1. Anti-oxidation

Rosemary has good antioxidant properties and is widely used in pharmaceuticals, food, and even fuel, with advantages such as non-toxic and non-side effects compared to synthetic antioxidants[37] . Ban et al. (2016) showed that rosemary extracts with high syringic acid content have high antioxidant activity and the components interact with each other[38] . Syringic acid can avoid lipid oxidation in vitro and can exert antioxidant effects not only at lower concentration levels, but also produce multiple coantioxidants in scavenging reactive oxygen species (ROS), forming a cascade reaction, which may enhance the antioxidant capacity of syringic acid and constitute an effective oxidative defense mechanism[39, 40] . HU Yan et al. (2015) showed that syringic acid in rosemary can be used as an antioxidant by activating silencing the mating-type information regulatory factor 2 homologous protein 1 (SIRT-1) pathway thereby reducing oxidative damage to hepatocytes by H2 O2 and inhibiting apoptosis during pathology[41] . Mezza et al. (2018) showed that rosmarinic acid can terminate the chain reaction of lipid peroxidation by competitively binding lipid peroxides; or inhibit the protein synthesis of inducible nitric oxide synthase (iNOS) and nitric oxide production, exerting antioxidant effects[42] . The antioxidant capacity of rosmarinic acid is determined by its structure The four phenolic hydrogens of rosmarinic acid share the ability to regulate free radical scavenging with two catechol fractions, which provide suitable polarity for rosmarinic acid to penetrate lipid bilayers and protect them from oxidation without damaging their structure[43-44] . In addition, Liu Fengxia et al. (2019) showed that the combination of rosemary liposol ursolic acid + oleanolic acid also exhibited some antioxidant properties in gardenia oil[45] . DIAS et al. (2015) showed that phenolics extracted from rosemary had better antioxidant effects on vegetable oils than tert-butylhydroquinone, which was previously considered the best anti-lipid oxidant[46] . Rosemary can be used not only for the preservation of edible oils but also to slow down the formation of harmful substances such as triacylglycerol oxidation polymers due to high temperatures during the cooking of soybean oil, thus improving the quality of edible oils as well as the food being cooked[47] . Chunxiu Lin et al. (2019) used the C. elegans model to study the anti-aging effects of sagittaria phenol, showing that sagittaria phenol can upregulate sod-3 , sod-5, hsf-1, hsp-16. 1 and hsp-16. 2 expression, and an increase in daf-16 translocation was observed, but daf-16 was not affected by sage phenol-induced lifespan. Experimentally sage phenol effectively reduced reactive oxygen species accumulation under normal or oxidative stress conditions and significantly increased several key antioxidant enzyme activities and lifespan of C. elegans[48] .

5.2. Antibacterial

The antimicrobial effect of rosemary is cytotoxic and can kill cells alone independent of the apoptotic mechanism, showing broad spectrum, sensitivity and concentration dependence.Nakassugi LP et al. (2015) showed that rosemary essential oil caused visible morphological changes in the mycelium of Fusarium oxysporum, and 150 mg /L of rosemary essential oil significantly inhibited its growth, and when Increasing the mass concentration to 300 mg/L caused cell wall rupture and cytoplasmic efflux[49] . Gauch LM et al. (2014) showed that rosemary essential oil also inhibited the formation of Candida albicans budding tubes, thereby inhibiting the oral inflammation caused by them[50] . Chifiriuc et al. (2012) used oleic acid/chloroform-coated rosemary essential oil to form microdroplets, and the experimental results showed that these microdroplets inhibited the attachment and biofilm formation of human Candida albicans and Candida tropicalis[51] . Liu Qian et al. (2019) found that rosemary essential oil stock solution had significant antibacterial effect on Staphylococcus aureus, Escherichia coli and Streptococcus by in vitro experiments; in vivo experiments found that rosemary essential oil inhibited Staphylococcus aureus colonization and showed significant antibacterial effect[52] .Miladi H et al. (2016) showed that rosemary essential oil alone had anti biofilm formation and its broad-spectrum antimicrobial activity when used alone or mixed with cinnamon

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essential oil in a certain ratio[53] . Masahiro T et al. (2010) showed that synthetic syringic acid has strong antibacterial activity against Propionibacterium acnes and drug-resistant Staphylococcus aureus, and it is speculated that syringic acid in rosemary may have the same antibacterial function[54] . Yuan Ganjun et al. (2012) demonstrated the significant anti-methicillin-resistant Staphylococcus aureus activity of syringic acid[55] . Bernardes WA et al. (2010) determined the antibacterial activity of rosemary stem and leaf extracts against Streptococcus pyogenes and Streptococcus salivarius and showed that the leaf extracts had higher antibacterial activity than the stem extracts, where syringic acid and syringol were the anti-streptococcal class of major active compounds[56] .

5.3. Anti-inflammatory

The mechanisms of the anti-inflammatory effect of rosemary include the maintenance of cell viability, inhibition of the production of immune factors, hindering the onset of enzymatic reactions induced by inflammatory factors, inhibition of lesion cell formation and inhibition of inflammatory cell aggregation, adhesion and migration. Figueira L W et al (2017) showed that rosemary extracts were effective against single and multiple microbial biofilms, showing anti-inflammatory effects by providing more than 50% (≤50 mg/mL) cell viability and no genotoxicity[57] . Liu Jundan et al. (2016) showed that rosemary extract prevented lipopolysaccharide-induced phosphorylation of mitogen-activated protein kinase and impeded activation of nuclear transcription factors, thereby reducing the expression of inducible nitric oxide synthase and cyclooxygenase-2 for anti-inflammatory effects[58] . Cheng Xian et al. (2015) showed that rosmarinic acid inhibits 5-lipoxygenase in arachidonic acid metabolism; inhibits the formation of complement-dependent lymph node lesions[59] . Sanchez et al. (2015) showed that rhamnol has significant anti-inflammatory and anti-catabolic effects on chondrocytes and may reduce cartilage matrix destruction by inhibiting IL-6 production by osteoblasts and promote the formation of subchondral osteoblasts[60] . Meanwhile, Yao Hui et al. (2017) showed that rhamnolol downregulates the ability of human umbilical vein vascular endothelial cells to adhere to lymphocytes and therefore has the potential to inhibit the recruitment, adhesion and migration of inflammatory cells in inflammatory bowel disease chronic inflammation of the intestine and has promise for the treatment of inflammatory bowel disease[61] .

5.4. Anti-tumor

The antitumor effects of rosemary are mainly carried out through participation in the apoptotic program, and the active ingredients of rosemary can inhibit cancer cell proliferation and induce apoptosis of cancer cells. Wang Wei et al. (2018) showed that rhamnol can block the biological activity of carcinogens, enhance the activity of antioxidant or detoxifying enzymes, inhibit tumor inflammation, inhibit cell proliferation and selectively induce autophagic apoptosis in cancer cells and can block tumor angiogenesis and invasion, thus showing chemopreventive effects against cancer[62] . Li Xin et al. (2018) showed that syringic acid can exert tumor suppressive effects and that syringic acid induces apoptosis by regulating the expression of apoptosis proteins[63] . Cheng et al. (2011) showed that rosmarinic acid can induce apoptosis in human colon adenocarcinoma cells through mitochondrial pathway and receptor-mediated pathway[64] . Huiling Zhou et al. (2018) showed that rosemary phenol can inhibit the proliferation of estrogen receptor-positive breast cancer cells (MCF-7) by blocking the value-added of proliferation in the S phase[65] . Wen R et al. (2018) showed that ursolic acid inhibited the proliferation of human liver cancer cells to varying degrees[66] . Molina S et al. (2014) showed that rosemary extract had antitumor activity against both colon and pancreatic cancer[67] . Mou Yishuang et al. (2015) showed that methylation of oncogenes is closely related to tumor development and rosmarinic acid can inhibit DNA methyltransferase activity for tumor chemoprevention .[68]

5.5. Anti-hyperglycemic

The active ingredients of rosemary can regulate blood glucose levels and can achieve a reduction in blood glucose concentration by promoting the uptake of blood glucose by myocytes. Elevated monocyte chemotactic protein-1 (MCP-1) and matrix metalloproteinase-9 (MMP-9) are partially responsible for diabetic vasculopathy.Naimi et al. (2017) showed that rosemary extract and rosemary extract polyphenols exhibit anti-hyperlipidemic and anti-hyperglycemic effects in genetic, chemically induced and dietary animal models of obesity and type 2 diabetes.Naimi et al. (2017) showed that rosemary extract and rosemary extract polyphenols exhibit anti-hyperlipidemic and anti-hyperglycemic effects[69] . Taekyung et al. (2014) showed that flavonoids and flavonoid phenolic acids in rosemary such as: gallic acid, caffeic acid and ferulic acid are potential inhibitors of α-glucosidase and can

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effectively inhibit postprandial blood glucose rise .[70] Ngo et al. (2018) showed that rosemary acid is a phenolic acid derivative of caffeic acid and therefore may also have hyperglycemic inhibitory effects[71]. Naimi et al. (2015) showed that low concentrations of rosmarinic acid promoted adenylate-activated protein kinase activation and increased glucose uptake in skeletal muscle cells, suggesting that rosmarinic acid may have anti-hyperglycemic biological properties[72]. These studies suggest that rosemary has the potential to be an antihyperglycemic agent.

5.6. Anti-neurological diseases

Lignans, syringic acid and rosmarinic acid in rosemary reduce the expression of heat shock protein 47 in nerve cells, thus ameliorating the degeneration of nerve cell damage in stressful environments[73] . Neurodegenerative diseases such as Alzheimer's disease (AD) , Parkinson's disease are generated due to the progressive loss of neurons in the brain or spinal cord. Meng P et al (2015) reported that degenerative deposition of β-amyloid is a pathological marker of Alzheimer's disease and syringic acid inhibits β-amyloid formation and its induced DNA repair enzyme poly(adenosine diphosphate) ribose polymerase (PARP) increase[74] , and Rasoolijazi H et al. (2013) reported that PARP plays an important role in DNA damage repair and apoptosis as a cleavage substrate for cystatin protease, a core member of apoptosis, suggesting that syringic acid has an interventional role in Alzheimer's disease[75] . Feng Maoxiao et al. (2020) reported that demonstrated Syringic acid enhances the binding of SNX17 to ApoER2 in a mouse model of AD, counteracting the negative effect of ApoE4 on ApoER2 cell surface levels, thus exerting a neuronal protective effect[76] . Filiptsova O V et al. (2018) reported that rosemary essential oil can improve memory in mice in a novel environment by stimulating the central nervous system, resulting in spontaneous activity and exploratory behavior significantly increased[77] ,

5.7. Other biological functions

In addition to the above biological effects, rosemary also has hypolipidemic, hypotensive, hypocholesterolemic, hepatosclerosis inhibiting, antithrombotic[78] , memory enhancing, antidepressant, antiviral and immune enhancing properties. In fact, many diseases are caused by oxidative damage.Fernández LF et al. (2014) reported , liver fibrosis caused by oxidative damage to the liver, neurodegenerative diseases caused by oxidative damage to the nerves, etc., and the antioxidant properties of rosemary are the basis for its potential physiological effects. Rosemary essential oil can clinically significantly increase blood pressure in patients with essential hypotension[79] . Al-Attar et al. (2014) reported that the use of thioacetamide (TAA) produced cirrhosis in Wistar rats (Wistar) and rosemary leaf extract inhibited the production of physiological and pathological histological alterations caused by TAA[80] . Raskovic A et al. (2015) Study reported that rosemary essential oil prevented carbon tetrachloride-induced increase in lipid peroxidation in mouse liver homogenates[81] . OI Aruoma et al. (1996) reported that a mixed extract of rosemary and Provence inhibited HIV infection but was cytotoxic at very low concentrations, while purified sage phenol exhibited definite anti-HIV activity at non-cytotoxic concentrations[82] . Paris A et al. (1993) reported that among the compounds such as rosmarinic acid, 7-O-methyl rosmarinic acid, and syringic acid, syringic acid also showed the strongest inhibitory activity against HIV-1 protease[83] . Zhao Xianmin et al. (2018) reported that rosemary essential oil improved memory function in mice with Alzheimer's disease[84] . Zhang et al. (2011) reported that rosmarinic acid has its anti-mutagenic activity effect[85] .

6. Conclusion

Rosemary contains a variety of bioactive components, mainly antioxidant, antibacterial, anti-inflammatory, antitumor, anti-hyperglycemic, anti-neurological diseases and other potential biological effects. The proportion of components varies greatly with the extraction site, preservation method, and processing method. With the continuous maturation of the extraction and purification process, rosemary will have a broad application prospect in the pharmaceutical, food and chemical industries. However, there is still a lack of research on the biological effects of rosemary, and there is still a need to further deepen the exploration. In addition, the cultivation and processing standards of rosemary in China are also inadequate and need to be further improved. Extraction methods are cumbersome, with large losses and unstable purity; the possible synergistic effects among the components of rosemary have not been explored.

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