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Mini Review

Polyphenolic Compounds of Wild Rosemary (*Rosmarinus officinalis L.*): From Extraction to Nanoencapsulation

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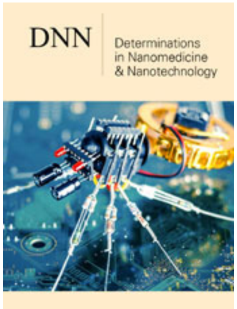

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Abstract

Encapsulation is becoming increasingly important in the pharmaceutical, food, cosmetics, textile, chemical, biotechnology and medicinal industries, particularly personal care and fragrances, due to its potential for stabilization and delivery of delicate and precious bioactive compounds. During the last decade there has been growing interest in the formulation of new cosmetic, food and pharmaceutical products containing natural compounds with antioxidant activity and other beneficial properties. Aromatic and medicinal plants have always been the major source of bioactive molecules. Especially, wild rosemary (*Rosmarinus officinalis L.*) which has been used since ancient times for its valuable health benefits that could be attributed to the richness of polyphenolic compounds, but these molecules are highly vulnerable to oxidants, light, heat, pH, water and enzymatic activities. Therefore, the stability and shelf life of phenolic compounds should be increased by being protected from chemical and physical damage by means of encapsulation prior to application. This mini-review provides an overview of recent advancements in nanotechnology to improve the loading efficiency of rosemary polyphenolic compounds in Silk Fibroin Nanoparticles (SFNs).

Keywords: *Rosmarinus officinalis L.*; Polyphenolic compounds; Silk fibroin nanoparticles (SFNs); Nanoencapsulation

Introduction

The use of herbs and plants has been of great interest, as they have been the sources of natural products, commonly named as bioactive compounds, with antioxidant potential and other beneficial properties. Specifically, the natural compounds from the *Lamiaceae family* (thyme, sage and rosemary) have been reported in several studies for their antioxidant, anti-inflammatory, antimicrobial and anti-carcinogenic activities [1-6]. In particular rosemary (*Rosmarinus officinalis L.*) has been widely accepted as one of the species with highest antioxidant activities of all the herbs and spices that have been investigated [7,8].

During the last decade there has been a growing interest in the formulation of new cosmetic, food and pharmaceutical products containing natural compounds with antioxidant and antimicrobial activities [9,10]. Unfortunately, due to their structure and nature, certain compounds such as polyphenols, are not stable and may interact easily with the matrices in which they are incorporated. Although it is crucial to benefit from the phenolic compounds, there are unsaturated bonds in the molecular structure of polyphenols and this makes them vulnerable to oxidants, exposure to light, heat, pH, water, and enzymatic activities [11,12]. Therefore, the stability and shelf life of polyphenolic compounds should be increased by being protected from chemical and physical damage prior to their application. Thus, the encapsulation is one of the strategies used to increase the stability and shelf life of these precious molecules. Encapsulation of phenolics components in carrier matrices has potential in the food, pharmaceutical, medicinal and cosmetics industries because it can provide protection against degradation, prevent loss of delicate and precious molecules, increase shelf-life and/or allow controlled release [11]. This study investigated the use of silk fibroin nanoparticles for encapsulating rosemary polyphenolic compounds.

Rosemary and polyphenolic compounds

R. officinalis L., a perennial herb that belonging to the *Lamiaceae family*, is native to the Mediterranean region and cultivated world-wide due to its use as a natural food preservative and flavoring agent. Rosemary has also been used as a source of traditional medicine for centuries; its applications have ranged from memory enhancement to the treatment of gastrointestinal diseases [1,2]. Rosemary extracts, mainly derived from the leaves, are common herbal products used as antioxidant and antibacterial agents in food processing and cosmetics. As naturally occurring antioxidants, they are preferred to synthetic antioxidants such as Butylated Hydroxyanisole (BHA) or Butylated Hydroxytoluene (BHT) [13]. Moreover, rosemary has been used in traditional and complementary alternative medicine for its digestive, tonic, astringent, diuretic and diaphoretic properties [14]. In Tunisia, *R.officinalis L.* is growing wild in bioclimatic zones extending from the sub-humid to the arid, with a rain fall level of 200 to 600mm/year on sandy, calcareous or marno-calcareous soils. This plant covers an area of about 340000ha. Leaves of this plant have been used for a long time in Mediterranean cuisine, not only to improve or modify the flavor of foods, but also to avoid its deterioration. Also, this plant is a symbol of remembrance and has been used since many centuries to improve memory. The infusion of leaves is used as antispasmodic, antiseptic, diuretic and relaxing. Dried leaves are used as additives to prevent fat oxidation and as flavoring agent in some meal [15]. This herb is the most used and economically important aromatic and medicinal plant for its essential oils and phenolic compounds [6,7].

Rosemary has been widely accepted as one of the spices with highest antioxidant activities of all the herbs and spices that have been investigated. Antioxidant activity of rosemary extracts depends on their composition. Several investigators found that rosemary contains diterpenes, such as carnosic acid and carnosol that characterized with its antioxidant activity. Also, several flavonoids and phenolic compounds, such as hispidulin, cirsimaritin, apigenin, genkwanin, naringin, caffeic acid and rosmarinic acid were found in rosemary extracts [1,6].

R. officinalis L. is among the most promising sources used for the recovery of essential oils through hydro distillation. Yet, the exploitation for polyphenols recovery from the residues that remain post-distillation, which may be used as antioxidant and antimicrobial agents in foods, food supplements or cosmetics, is really limited. Nevertheless, some previous studies have that the post-distillation wastes materials from rosemary still possess antioxidant and antimicrobial activities [16]. Furthermore, the residues remaining after essential oil recovery, which is currently disposed of as waste, have been studied for their content of a diversity of biologically active compounds, including antioxidants such as phenolic acids and flavonoids [1,2,6]. The antioxidant and antimicrobial activities of rosemary are mainly attributed to its phenolic compounds, including rosmarinic acid, Cainozoic acid, rosmanol, carnosol, and epirosmanol. In general, it has been reported that the antioxidant activities have a high correlation with the content of flavonoids and phenols [10].

Nanoencapsulation

In order to minimize aroma degradation or loss during processing and storage, it is beneficial to encapsulate bioactive molecules prior application. Encapsulation is becoming increasingly important in the pharmaceutical, food, cosmetics, textile, personal care, chemical, biotechnology and medicinal industries due to its potential for stabilization and delivery of volatile and delicate and precious bioactive compounds. The field with the highest level of encapsulation applications is the drug sector (68%), followed by food (13%) and cosmetics (8.0%) [17]. In addition to stabilizing and protecting encapsulated flavors, fragrances, oils and phenolic compounds encapsulation may also be able to provide controlled release under desired conditions. Controlled release may be defined as a method by which one or more active agents or ingredients are made available at a desired site and time and at a specific rate. This precise timing and targeting of release could be used to maximize a given compound's effectiveness and optimize dosage [18].

Though many materials have been proposed for encapsulation in food, cosmetic and medicinal applications, silk is a highly versatile protein utilized in the textile, cosmetic, and chemical industries. Recently, it has also been developed for use in a broader range of biomaterials and regenerative medicine needs, as well as for cell encapsulation and controlled drug delivery systems. Silk is a natural polymer product; a relatively inexpensive, biocompatible, biodegradable, and non-toxic FDA-approved protein derived from the Bombyx mori silk worm cocoon. Fibroin has recently been investigated in the drug field carrier for controlled release [6,18,19]. During the last few decades, their use has also been spread in a broad range of applications in regenerative medicine as a scaffold for tissue engineering, as well as in nanomedicine as controlled drug delivery systems. Their extensive hydrogen bonding, amphipathic nature and high degree of crystallinity contribute to the stability of silk biomaterials. Formulated as particles, Silk Fibroin (SF) is used in nanomedicine for its capacity to act as a reversible carrier of bioactive molecules [20,21]. Although SF has been investigated as a carrier for single antioxidant molecules as resveratrol, quercetin, or curcumin among others, for volatile compounds, and for vegetal oils in the form of emulsions [22]. Also, Silk Fibroin Nanoparticles (SFNs) have become a promising tool in drug delivery systems due to their physicochemical proprieties and have shown their outstanding properties as an active vehicle for polyphenols, enhancing their antioxidant and anti-inflammatory effects on macrophages [18].

Rosemary hexane extract-loaded lipid nanocapsules based gel provided photoprotection, restored the antioxidant biochemical state, improved epidermal and dermal histological features, and decreased the level of inflammatory and wrinkling markers [21]. The Rosemary Methanolic Extract (RME) loaded into silk Fibroin Nanoparticles (SFNs) and the free SFNs as control was investigated and the DPPH scavenging activity assay confirmed that the activity antioxidant of the RME loaded into the SFNs were better preserved in comparison with the free RME. This effect has been previously described for silk fibroin nanoparticles due the strong interactions between the phenolic compounds and the silk fibroin [6]. Thus, further experiments are needed in order to improve the efficiency of the rosemary extracts nanoencapsulation.

Conclusion

A bioactive compound encapsulated in Silk Fibroin Nanoparticles (SFNs) can be efficiently protected from harmful environmental agents like light, oxygen or water. The use of silk aqueous solution allows the final materials to be all natural, biocompatible, controllable in terms of properties and protected against the degradation. Thus, nanoencapsulation is one of the strategies used to increase the stability and shelf life of bioactive molecules. Nanoencapsulation not only permits the polyphenolic compounds from medicinal and aromatic plants to be stored, but also to be recovered under specific conditions and controlled release. The silk fibroin nanoparticles loaded with rosemary polyphenolic compounds had an effective potential as natural antioxidant and seemed to be a promising combination for several applications in food technology, pharmaceutical industry and nanomedicine. Thus, further experiments are needed to confirm that SFNs represent a highly customizable material with great potential in biomedical applications due to their mechanical and physicochemical properties.

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