Liposomal Saffron: A Promising Natural Therapeutic and Immune-Boosting Agent

Saffron is the commercial name of the dried stigmas of *Crocus sativus* flower, commonly known as the "saffron crocus." The colorful crimson stigma and styles (called threads) are collected and dried for use, generally as an aromatic seasoning and coloring agent in food. The main ingredients of saffron include crocin, safranal, picrocrocin, and crocetin which are primarily recognized for their antioxidant and therapeutic properties. These bioactive compounds possess various therapeutic and organoleptic properties, which are as follows: (i) they are powerful antioxidants, (ii) promote digestion, (iii) improve mood and treat depressive symptoms, (iv) have cancer-fighting properties, (v) reduce symptoms of premenstrual syndrome, (vi) act as aphrodisiac, (vii) reduce appetite and aid weight loss, (viii) boost immune system, and (ix) improve eye sight. Moreover, nanoencapsulation of these bioactive ingredients is a novel platform to boost the therapeutic efficiency and inhibit degradation of saffron bioactive compounds.[1,2] Human cultivation and application of saffron dates back to more than 3500 years. Although some doubts remain on its origin, it is suggested that saffron originated in Iran, nonetheless, Greece and Mesopotamia have also been suggested as the possible origins of this plant.[3] Saffron flowers, stigma, and filaments are being used as medicinal ingredients for a long time. To illustrate this, the abortive action of the ingredients of saffron was well known in the middle ages, during which it was also used by midwives in deliveries for the sedative and antispasmodic properties of the plant.[4] Besides, it has been employed to treat eye diseases, heal wounds, fractures, and joint pains and for many other uses, leading to Pliny the Elder describing it as a kind of panacea in his Naturae Historiarum XXXVII.[4] Saffron bioactive components have demonstrated anti-inflammatory and anti-fibrosis activities in clinical trials.[5] Furthermore, it is reported that saffron bioactive compounds are effective against suppression of tumor cells.[6] With the emergence of COVID-19, the production of immune-boosting supplements has increased significantly. Interestingly, it is reported that crocetin has a high affinity toward spike protein of COVID-19 virus (the main polypeptide of the virus), thus can hinder the access of the virus to the cell receptor.[5] Due to the low stability and sensitivity of the saffron bioactive ingredients, the encapsulation technology has surmounted this grave problem. In short, encapsulation comprises a shell to protect particular ingredient(s) and to prevent them from leaching out before reaching the target site.[7,8] Accordingly, one of the interesting technologies for encapsulation purposes are liposomes and its derivatives including nanoliposomes, tocosomes, and solid-lipid-nanoparticles, which are affordable, stable, and simply produced.[9,10] Encapsulated saffron ingredients, using emulsions, liposomes, or their derivatives, are promising candidates for the production of food supplements and immune-boosting products, which has captured the attention of both industry and academia, particularly in the pandemic era.[11,12] Balanced and healthy food along with dietary supplements are extremely important in decreasing the rates of mortality and morbidity associated with viral and other diseases such as cancer. It is well known that dietary supplements and nutraceuticals play a very important role in the preventive as well as curative aspects of viral and nonviral diseases.[13] Conventional manufacture of lipidic encapsulation systems required use of potentially toxic solvents (e.g., chloroform, methanol, and diethyl ether). Thanks to recent progress in the field of encapsulation, these lipidic systems can now be manufactured, without utilization of toxic solvents or detergents, on large scales. Examples of such methods include the "heating method"[14] and "Mozafari method."[15] Loading saffron to liposomes or nanoliposomes using Mozafari method can be accomplished through the following three steps:

1. Adding capsule ingredients to a preheated (60°C) mixture of saffron and a cosolvent such as glycerol, sorbitol, or propylene glycol (final concentration 3%, v/v) in a heat resistant vessel.
2. Heating the mixture at 60°C while stirring (e.g., 1000 rpm) for a period of 45 to 60 min under an inert atmosphere (e.g., using nitrogen gas).
3. Following preparation of the formulation, it must be kept at temperatures above phase transition temperature of the phospholipid ingredients (Tc) under an inert atmosphere for 1 h to allow the vesicles to anneal and stabilize [Figure 1].[15]

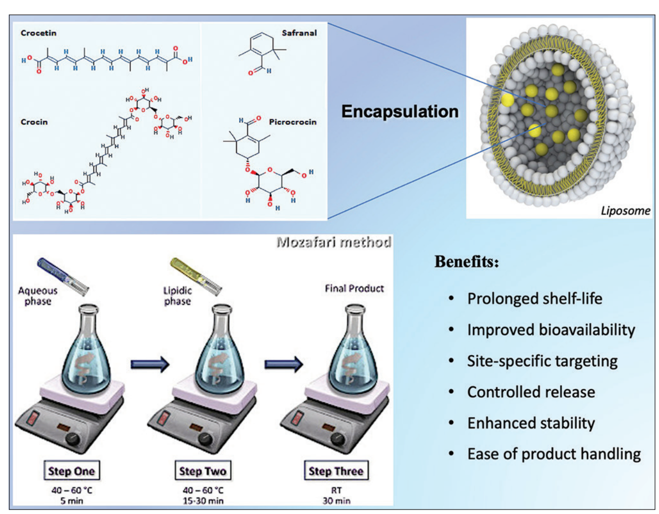

Figure 1: Schematic representation of simple and green-tech methodology of liposomal encapsulation of saffron active molecules and its benefits

Last but not least, the green nature of both saffron and liposomes makes them attractive candidates for application as edible products and undoubtedly soon the market of this high-tech product will grow remarkably.

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Conflicts of interest

There are no conflicts of interest.

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