

Nowadays, there is a huge interest on natural products that can promote the state of health and well-being for humans. A sample collected from the area of Olympus mountain exhibited significant protection against the cytotoxic effects of UVB radiation by remarkably reducing DNA and protein oxidation damage levels in human immortalized keratinocyte (HaCaT). Ong et al. [24] prepared a chitosan–propolis nanoformulation based on optimum physicochemical properties such as particle size, zeta potential, polydispersity index, encapsulation efficiency and the rate of release of the active ingredients for biofilm applications. As far as the encapsulation of propolis is concerned, Zhang et al. [23] developed propolis loaded zein/caseinate/alginate nanoparticles that demonstrated a promising clean and scalable strategy to encapsulate propolis for applications in foods, supplements and pharmaceuticals. The particular properties of both carriers that were taken in advantage are: The ability of the cyclodextrins to enclose polyphenols and enhance their permeability through the skin [38][39] as well as the ability of the liposomes to encapsulate large quantities of components of various degrees of polarities, for topical transport of components and control of their release rate [40][41][42]. It also demonstrated significant antiaging efficacy as it decreased histological damage and lowered the induced expression of certain metalloproteinases (MMPs) following exposure to UVB in a reconstituted skin model [43]. The complexity of the structure of propolis combined with the variable composition depending on the region and the collection season make both raw propolis and its extracts particularly difficult to formulate into products for per os or skin applications [6][16]. This copolymeric matrix system was able to encapsulate different flavonoids from red propolis extract with interesting characteristics of solubility and antioxidant activity demonstrating activity against leishmaniasis. Tao et al. [27], investigated the immune modulatory function of propolis flavonoids encapsulated in liposomes and showed the potential of the application of the formulation as an adjuvant. Ishida et al. [34], complexed caffeic acid phenethyl ester from propolis with  $\beta$ -cyclodextrin in order to increase the stability of the former that gets easily degraded by esterases. Liposomes loaded with cyclodextrin–bioactive molecule complexes are widely used as drug delivery systems, enhancing low aqueous solubility and stability [36][37]. It exhibits antimicrobial, immunostimulatory and antioxidant activity and is employed in the preparation of functional foods and cosmetics as well as in traditional medicine [2][5][6][7]. The extraction of propolis usually has a low yield in active component concentration [17][18], especially when natural solvents, as water or vegetable glycerol are used. Arafa et al. [28], prepared oromuco–adhesive films for buccal delivery of propolis entrapped in niosomes. Vasilaki et al. [33], prepared extracts of propolis by using aqueous solution of hydroxypropyl– $\beta$ -cyclodextrins as an alternative for food preservation. Based on our previous studies we have identified promising propolis extracts collected from different areas in Greece. All bee products—honey, royal jelly, propolis, bee pollen, beeswax and even bee venom—have been largely investigated for their healing properties [1][2][3][4]. It contains approximately 50% resins, 30% waxes, 10% aromatic components, 5% pollen and 5% various other components [2][8][9]. The bioactive components of propolis are polyphenols, terpenes, steroids, as well as sugars and aminoacids [10][11][12][13][14][15].  $\beta$ -cyclodextrin was also used by Rimbach et al. [35] for the encapsulation of Brazilian green propolis supercritical extract. In the present study, an extraction and encapsulation of components of propolis in a combinatorial liposome–cyclodextrin system is performed. The extracts

demonstrated significant in vitro antioxidant activity due to their high total phenolic and flavonoid content. Propolis is a resinous substance which is produced by bees and presents many challenges in respect to its extraction and formulation process. Its composition varies depending on the flora of the foraging region of the bees and the collection season. In order to increase the extraction yield, various extraction methods have been developed [19][20] as well as methods of encapsulating its components in various carriers [21][22]. Aytakin et al. [26], developed a propolis loaded liposomal system that showed interesting results as a topical application in wound treatment having antioxidant and antimicrobial effects.