CHITOSAN FILMS WITH QUERCETIN FOR SKIN APPLICATIONS

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Abstract

The release of active compounds is widely studied for both biomedical and cosmetic applications. Special attention is paid to the delivery of antioxidative compounds, which act as antiaging agents and thus protect the skin and help in the wound healing process. This paper presents the results regarding the fabrication of chitosan-based films for the release of quercetin. Chitosan was modified by introducing a small amount of hyaluronic acid, and then quercetin was added. Thin polymeric films were fabricated using the solution casting method. The obtained films were analyzed using FTIR spectroscopy and thermal analysis. Surface properties have been studied using an AFM microscope. The roughness of the films was changed after the addition of hyaluronic acid and quercetin to the chitosan films. HPLC was used to analyze the release of quercetin from the polymer film. The maximum release of quercetin was found after 20 min at pH 5.5, which is the pH of normal human skin. The average percentage of the release of quercetin from the films based on chitosan was 21.62 ± 0.50%, whereas from the chitosan/hyaluronic acid film, it was 27.07 ± 1.96%. The results suggest that the proposed films with incorporated quercetin show potential as materials for wound healing and beauty masks due to their antioxidative properties.

Keywords: *chitosan, quercetin, films, cosmetics, skin, beauty mask*

Introduction

In recent decades, pharmaceutical and cosmetic technologies have focused on novel delivery systems for active substances [1]. For this reason, synthetic polymers and biopolymers are widely studied for acting as carriers for active substances, providing modified release according to the needs. Active substances used in pharmaceutical and cosmetic technologies can be of natural or synthetic origin. Among active substances of natural origin, flavonoids are widely used in the pharmaceutical and cosmetic industries [2-4]. They are used as ingredients, especially in antiaging cosmetics, according to their antioxidant properties [5-7]. The antioxidant properties can be useful as part of a diet [8,9] and in several biomedical applications [10-13]. In a wide group of flavonoids, quercetin is considered an anti-aging component of cosmetic formulation for topical application on the skin [8-10]. The structure of quercetin is presented in FIG. 1. The ageing of the skin is a complex biological process that is influenced by several endogenous and exogenous factors. Several anti-ageing strategies have been developed during the last few years. The use of antioxidants is one of them. Other strategies include preventive measurements, cosmetological strategies, topical and systemic therapeutic agents, and invasive procedures. A thorough review of skin anti-ageing strategies has been conducted by Ganceviciene et al. [14].

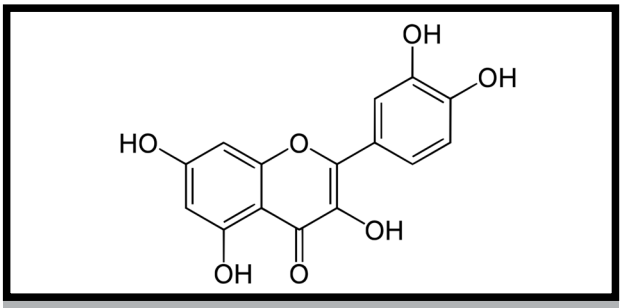

FIG. 1. The structure of quercetin.

Quercetin is a dietary flavonol commonly found in fruits, vegetables, and nuts [15,16]. It can occur in many different glycoside forms [15]. The main dietary sources of quercetin are lettuce, chilli peppers, cranberries, onions, black chokeberries, elderberries, capers, tomatoes, broccoli, apples, and some others [16]. The role of natural compounds in cosmetic formulations is widely shown in the scientific literature [17-21]. Numerous modified dosage forms of quercetin, most notably nanoparticles, microemulsions, and other carriers, have recently been developed for both pharmaceutical and cosmetic applications [20,21].

Cosmetic and pharmaceutical formulations have come a long way over the years and continue to evolve. Cosmetics are expected to bring additional benefits to the skin, not only in terms of appearance but also in terms of health. For this reason, cosmetic masks containing active ingredients are becoming increasingly popular [3,6,7]. The cosmetic market is seeing an increase in interest in using biodegradable materials and ingredients of natural origin. Natural products can offer several advantages over synthetic ingredients. Thanks to natural ingredients (e.g., flavonoids, phenolic acids, alkaloids), natural cosmetics often have a broader spectrum of action than cosmetics produced based on synthetic ingredients [22,23]. In this study, chitosan films were obtained containing a natural biologically active compound - quercetin. We have been motivated by the fact that in recent years, interest in chitosan in cosmetic and pharmaceutical formulations has been constantly growing, especially in terms of its use in the production of cosmetics and wound healing materials [9]. The incorporation of quercetin into polymer films or membranes may be an excellent alternative option for delivering this active compound to the dermal layer. To date, several polymers have been used as carriers of active substances for cosmetic applications [22-26]. However, there are some limitations to their use, including, but not limited to, problems such as cytotoxicity and lack of biocompatibility that can occur when using polymer-carriers in controlled delivery systems for bioactive substances [1,25,26]. The interest in chitosan as a component of cosmetic and biomedical products is related to its film-forming and antimicrobial effects [27-31].

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The state of the art regarding materials based on chitosan and quercetin shows that such a combination is proposed for wound healing and cancer treatment [32,33]. The review regarding the use of various polymers in delivering quercetin has been published by Kurniawan et al. [34]. It has been mentioned that developing a quercetin delivery system using composite polymers presents both an opportunity and a challenge for future applications. In our research, we used chitosan with the addition of hyaluronic acid to prepare films that can be used as a base for cosmetic masks, and this is a novelty of our research. To our knowledge, such compositions have not been studied yet.

The main hypothesis was that quercetin loaded into chitosan-based films may exhibit new, promising properties, including increased bioavailability. The use of such a cosmetic mask or occlusive material will allow for obtaining a cosmetic that creates a new way of releasing a bioactive substance (quercetin) into the skin. The slow release of quercetin in the first stage only from the mask surface and then from deeper layers will enable more effective use of this active substance (bioavailability). Similar studies were conducted on silk fibroin. The results of the study indicated that silk fibroin nanoparticles improve the immunomodulatory properties of quercetin in DSS-induced colitis in mice [35]. Although these were studies on the use of quercetin in medicinal preparations, it seems to that the effect of the slow release of quercetin from chitosan film may result in its better use to improve the condition of the skin. Therefore, we proposed that the combination of quercetin and chitosan can lead to the production of good quality cosmetic masks with antioxidant and, therefore, anti-ageing properties.

Materials and Methods

Materials

In the research, we used chitosan (CS) with an average molecular weight of 1,113,000 g/mol (according to the manufacturer's declaration) and a degree of deacetylation of 75% lactic acid ($C_3H_6O_L$), and pharmacopoeial grade quercetin were purchased from Sigma-Aldrich (Poznań, Poland). The supplier of pure anhydrous glycerin (GLY, $C_3H_8O_3$) was Chempur (Piekary Śląskie, Poland). The hyaluronic acid (HA) used in the studies was of cosmetic grade (purchased from a local cosmetic company Proszkowice, Poland). The chemical structure of the biopolymers was checked by IR analysis. All chemicals were used without further purification.

Preparation of polymer films modified by quercetin

Chitosan solution (2% w/v) was obtained by dissolving an appropriate amount of solid chitosan powder in 0.3 mol/dm^3 lactic acid water solution. The dissolution process was carried out at room temperature (25 ± 1°C) for 72 h. Lactic acid (LA) was chosen because it is quite often used in cosmetic formulations for pH modification. Moreover, its addition makes it possible to dissolve chitosan (CS is insoluble in water). In the next step, glycerin, quercetin, and hyaluronic acid were added to the chitosan solution, and polymeric films were fabricated. Glycerin was added to the chitosan solution in a ratio of 0.5:1 to chitosan powder. Quercetin powder (QRC) and hyaluronic acid solution (1%) were added in a ratio of 1% w/w (relative to chitosan). The prepared mixtures were mixed at 100 rpm for 24 h. The chitosan-based films were fabricated by solution casting method (32 ml of polymer solution was poured into square Petri dishes with size 100 × 100 × 15 mm). The casted films were allowed to air dry for 3 days prior to further characterization. In this way, three thin films were obtained: CS/GLY, CS/GLY/QRC, and CS/GLY/QRC/HA. The composition of the studied films can be seen in TABLE 1.

TABLE 1. Components of CS-based liquid formulations for film fabrication.

Components	CS/GLY [% w/w]	CS/GLY/QRC [% w/w]	CS/GLY/QRC/HA [% w/w]
CS	1.96	1.98	1.96
GLY	2.06	1.06	0.98
QRC	-	0.02	0.02
HA	-	0.00	0.02
LA	2.64	2.63	2.60
water	to 100	to 100	to 100

The film thickness was measured using a hand micrometer (Sylvak) with a measurement accuracy of 0.001 mm. At least seven random locations on each film were used for the measurements, and the values were reported as mean ± standard deviation (SD).

Infrared spectroscopy

The chemical structures of the biopolymers and interactions between components in the polymer blend were studied by infrared spectroscopy. FTIR spectrometer (Nicolet iS10, Thermo Fisher Scientific, Waltham, MA, USA) connected to a total reflection attenuation unit (iDe-Ge-ATR) was used. One hundred scans were performed for each measurement with a spectral resolution of 2 cm^{-1}. The spectra were recorded in the range of 4000-400 cm^{-1}. The obtained ATR-FTIR spectra of the tested films were analyzed using Omnic 9.3.30 software (Thermo Fisher Scientific, USA).

Morphological properties

For surface characterization, an atomic force microscope was used (Nanoscope IIIa Multimode Scanning Probe Microscope, Digital Instruments, Veeco Metrology Group, Santa Barbara, California, USA). The analysis was done in a tapping mode, under ambient conditions. The mean square (Rq) and arithmetic mean deviations of the recorded profile (Ra) were determined from the AFM images (10 µm × 10 µm) using NanoScope Analysis v1.40 software (Bruker, Ettlingen, Germany).

Thermal analysis

For thermal analysis, the SDT 2960 Simultaneous TGA-DTA analyzer from TA Instruments (TA Instruments Manufacturing, Eschborn, Germany) was used. Measurements were performed in the temperature range from 20°C to 600°C. The heating rate was 20°C/min. Measurements were performed in a nitrogen atmosphere.

The release of quercetin from a biopolymeric film

The release of quercetin (QRC) from the obtained biopolymer films was studied at pH 5.5, which is a typical pH value of the human skin. For this, a phosphate buffer was used. The films were cut into pieces of 4 cm^2 (length × width = 2 cm × 2 cm) and weighed on an analytical balance. The weighed pieces of film were immersed in a round-bottomed flask containing 50 ml of phosphate buffer. The flask was placed in a heating jacket with stirring. The temperature during the release process was maintained at 35.5 ± 1°C, similar to human skin. After selected release times (1; 3; 5; 10; 15; 30; 45; 60; 90; and 120 min), 1.5 ml of solution was taken for analysis.

The concentrations of quercetin in 1.5 mL of buffer were measured using the liquid chromatography technique. For this HPLC system equipped with an autosampler SIL-20AC HT and a photodiode multi-wavelength detector (SPD-M20A Prominence Diode Array Detector), SHIMADZU (Japan) was applied. Quercetin was detected by a photo-diode array detector at 254 nm. Analyses were carried out with column 250/4.6 Nucleoshel RP 18. As a mobile phase, a 1:1 water: 2% acetic acid mixture was used. The rate-flow was 0.8 ml/min. The volume of the sample was 20 µL. The samples were analyzed at 25 ± 1°C. Before release measurements, the calibration curve for the determination of the quercetin concentration was prepared (FIG. 2).

The linearity of the method was found in the range from 1.13 to 22.6 mg/L ,and the obtained calibration curve equation was y = (78348 ± 3952)x + (-33150 ± 46460) with determination coefficient R^2 = 0.9992. The calculated limit of detection and limit of quantification were 1.16 mg/L and 2.69 mg/L, respectively.

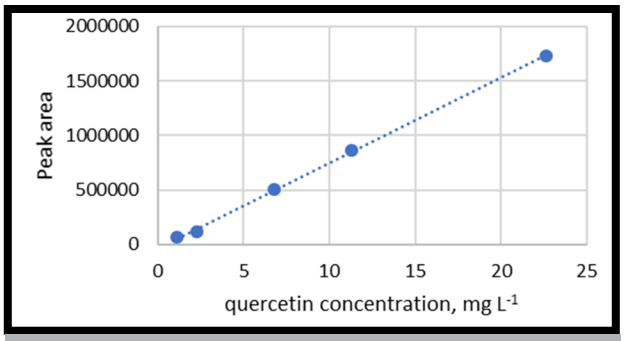

FIG. 2. Calibration curve for the determination of quercetin.

Results and Discussions

Infrared spectroscopy

The FTIR-ATR analysis was performed to investigate the molecular structure of chitosan and chitosan films with quercetin. In addition, FTIR analysis allowed the observation of the presence of functional groups, which can be used to identify compounds and possible interactions between the components of the material. The spectra of pure quercetin and the film prepared based on chitosan obtained in this study are shown in FIG. 3.

In the QRC spectrum in the region from 1662 cm^{-1} to 1449 cm^{-1} the bands assigned to the C=O group and aromatic ring, respectively, were observed [36]. For the biopolymer film, the characteristic bands for chitosan were observed in the FTIR spectra. The stretching vibration of -OH and -NH group occur at 3264 cm^{-1}, while the -CH stretching vibrations band is at 2930 cm^{-1} and -CH stretching vibrations band in the pyranose ring at 2880 cm^{-1}. Other bands which are related to the amine I band at 1646 cm^{-1}, the amine II band at 1575 cm^{-1}, and the amine III band at 1456 and 1374 cm^{-1} were also observed. The band at 1120 cm^{-1} and the bands at 1076 and 1030 cm^{-1} can be assigned to the β-1,4-glycoside and the C-O-C, C-O, and C-OH vibrations, respectively [37,38]. Moreover, in the spectra of the studied films the bands which are characteristic of lactic acid (at 1125, 1220, and 1722 cm^{-1}) were identified [39,40]. A wide peak around 3500 cm^{-1} is due to the water absorption of the specimen.

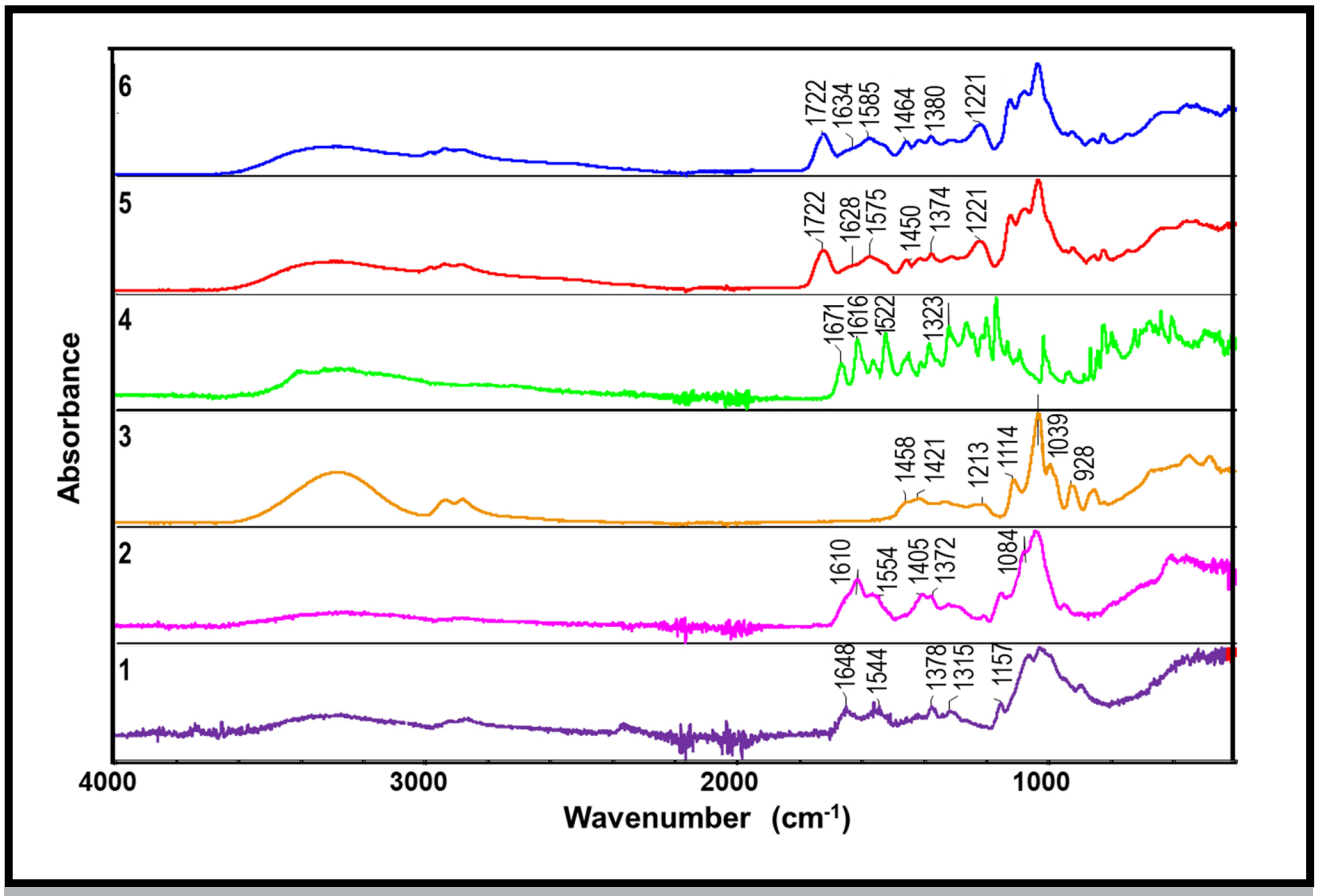

FIG. 3. FTIR spectra of CS (1), HA (2), GLY (3), QRC (4), CS/GLY/QRC (5), and CS/GLY/QRC/HA (6).

The position of amine II and amine III in the chitosan spectrum is not altered by the addition of quercetin. The shift of the position of amine A and amine B was observed. Such a shift of bands may suggest the formation of hydrogen bonds between chitosan and quercetin. It should be noted that the chitosan-based film prepared in this study also contained hyaluronic acid and glycerol. The above ingredients were used to obtain flexible and pliable films suitable for cosmetic applications. A small amount of hyaluronic acid was added to chitosan to obtain films with better functional and physicochemical properties [41]. The IR spectra for quercetin (spectrum 4 in FIG. 3) were registered for a powder; for this reason, this spectrum shows a slightly different structure.

Thermal stability

The thermal properties of materials are important when thermal sterilization is used before the final use of polymer-based materials. Thermal stability is also important for the use of natural polymers in both pharmaceutical and cosmetic applications. For this reason, the thermal stability of newly fabricated materials is assessed based on thermogravimetry. The TG analysis was performed for the two obtained films CS/GLY/QRC, and CS/GLY/QRC/HA. In addition, thermogravimetric analysis was also performed for all components of the fabricated films: chitosan, hyaluronic acid, glycerol, and quercetin. The thermogravimetric curves of chitosan films containing quercetin are shown in FIG. 4.

In the TG curves, three regions can be distinguished. The first one is mainly correlated with the water elimination from the sample. This process for both films started at 50°C but for CS/GLY/QRC/HA T_{max} values were observed at 85°C, while for CS/GLY/QRC at 100°C with T_{max} values 101°C. The peak area in this region responsible for water elimination was significantly larger for the CS/GLY/QRC/HA film than for the CS/GLY/QRC film. This indicates a stronger water binding in the film produced without hyaluronic acid. The initial mass loss for both films was about 7% (w/w). The second peak can be correlated with the degradation of the components used. The T_{max} for the CS/GLY/QRC/HA film was 210°C, while for the CS/GLY/QRC film it was 225°C. The mass losses calculated at this stage are similar and amount to about 35% for both analyzed samples, but it can be easily seen that the GLY/QRC/HA film degrades faster than the CS/GLY/QRC film.

The third peak in the TGA curve is due to chitosan pyrolysis. T_{max} at 300°C for all materials was comparable, but the peak area for CS/GLY/QRC/HA film was larger than for the other film. This may suggest that the interactions between components in CS/GLY/QRC/HA films are much stronger than in the polymer film with the composition of CS/GLY/QRC [37,40].

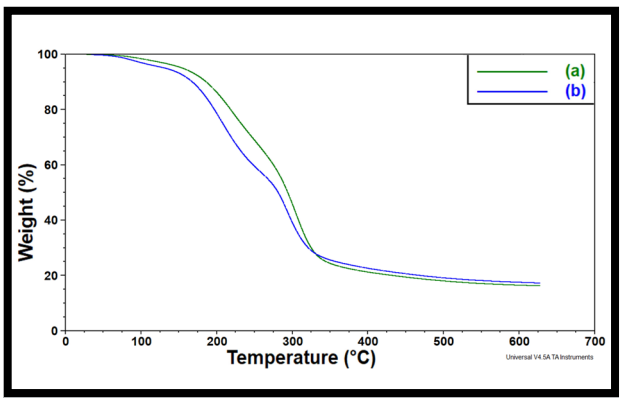

FIG. 4. TGA curves of the prepared films: a) CS/GLY/QRC; b) CS/GLY/QRC/HA.

Morphology

Atomic force microscopy (AFM) was used to evaluate the surface properties of the obtained biopolymer films. In FIG. 5 the AFM topography of the films is shown.

As can be seen (TABLE 2), the roughness parameters calculated from the AFM experiment for CS/GLY, CS/GLY/QRC, and CS/GLY/QRC/HA films differ. The highest roughness was found for the CS/GLY/QRC film. The surface of the CS/GLY/QRC film was characterized by higher Rq parameters (root mean square deviation of surface roughness) than for other samples. The surface roughness increased after the addition of quercetin to chitosan. Adding HA led to a further increase in surface roughness. This may be due to the incomplete dissolution of quercetin in the chitosan solution.

The release of quercetin from a biopolymeric film

In FIG. 6, the release profiles of QRC from CS/GLY/QRC and CS/GLY/QRC/HA films are shown. The release was carried out at pH 5.5. The pH value of 5.5 is typical for human skin, so the in vitro release process of quercetin in this condition may mimic the release after the application of the mask on the skin [15]. As can be seen in FIG. 6, the release of QRC is different for both films studied. It is known that the active substance can interact with the matrix. This interaction influences the diffusion of the active substance in the material [42,43].

As shown in FIG. 6, the maximum concentration of quercetin released from the tested films was observed after 20 min at pH 5.5. The average percentage of quercetin release from the CS/GLY/QRC film was 21.62 ± 0.50%, while from the CS/GLY/QRC/HA film, it was 27.07 ± 1.96%. The results show, that in the presence of HA, the interaction of QRC with chitosan is smaller. It can be due to the interaction of HA and chitosan. In the structure of HA, there are groups active in further modification, such as carboxyl groups, hydroxyl groups and -$NHCOCH_3$ groups [34-38]. Carboxyl groups and hydroxyl groups can form hydrogen bonds between two biopolymers and also with the active substance. The observed release of quercetin from chitosan films containing HA may be due to the fact that quercetin is additionally bound by hyaluronic acid.

Discussion

Quercetin is used in cosmetics mainly for its antioxidant properties [8-13]. Experiments using quercetin against melanogenesis have also been conducted *in vitro* [44]. The antimelanogenesis effect of quercetin is not clear but probably depends on the concentration of quercetin in the formulation [45]. Considering the literature reports, quercetin has skin protective properties against damage caused by UV radiation. The application of QRC led to reduced redness and inflammation. The skin barrier can be restored, which can lead to increased skin hydration [13,14]. However, the stratum corneum shows low hydrophilicity. It may be a reason for poor percutaneous absorption and thus significant limitations of conventional topical administration of quercetin [46]. The incorporation of quercetin into polymer films or membranes may be an excellent alternative option for delivering this active compound to the dermal layer. Several polymers have been used so far as carriers of active substances for cosmetic applications [37-43]. As mentioned in the introduction, there can be some limitations in using polymers. e.g. problems with cytotoxicity and low biocompatibility that may occur when using polymer-carriers in controlled delivery systems for bioactive substances [1,25,26]. In our study, a biopolymer blend based on biocompatible polysaccharides, chitosan, and hyaluronic acid (biodegradable and eco-friendly), was used. The fabricated films can be easily used as a base for cosmetic masks.

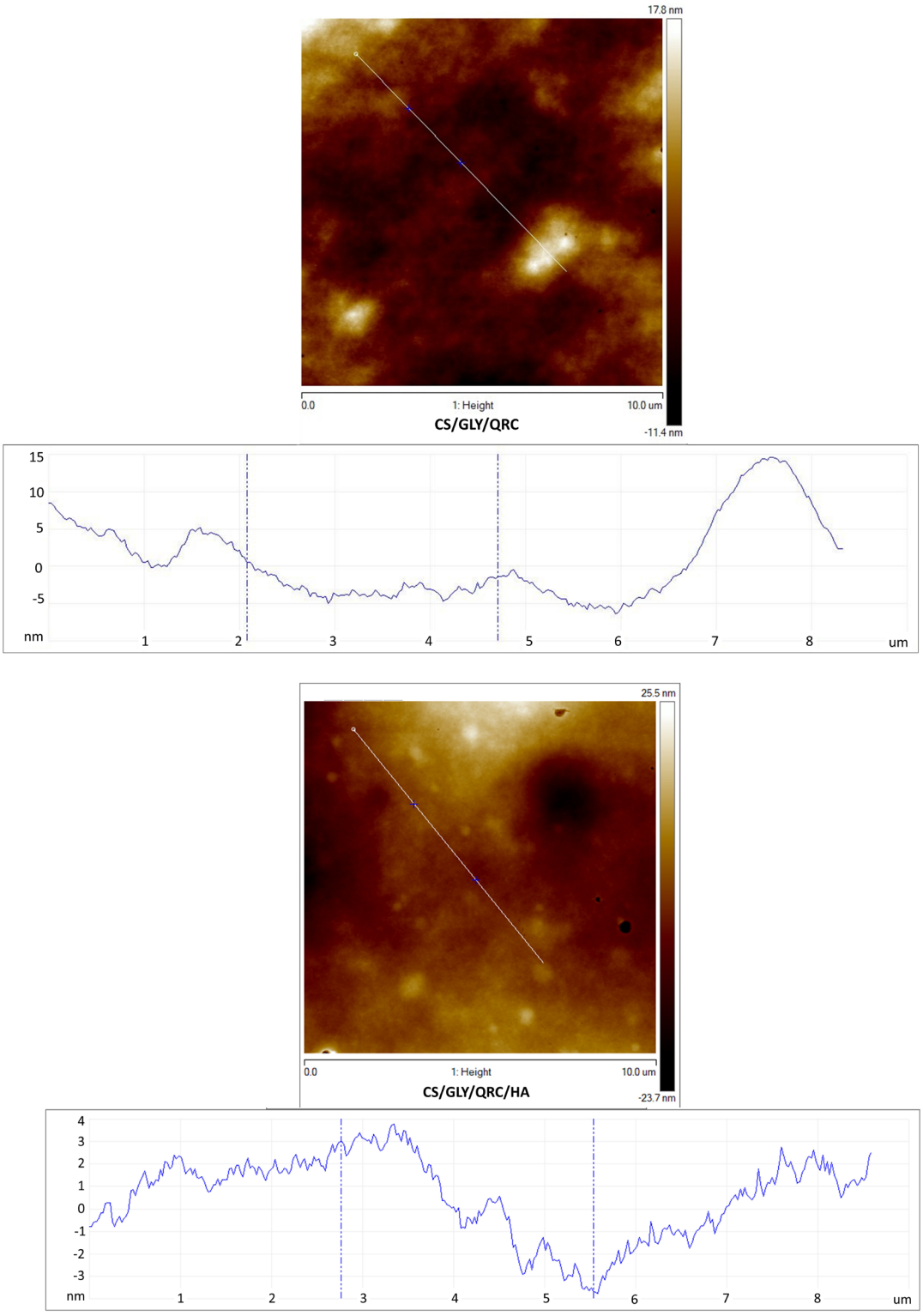

FIG. 5. AFM images and topography of obtained CS-based films.

TABLE 2. Roughness parameters (Rq and Ra) and thickness (Th) for films with various compositions.

Sample	R_q [nm]	R_a [nm]	Th [mm]
CS/GLY/QRC	3.19 ± 0.21	2.15 ± 0.19	0.075 ± 0.005
CS/GLY/QRC/HA	3.88 ± 0.23	2.28 ± 0.15	0.071 ± 0.004

Choudhary et al. [47] prepared chitosan nanoparticles bound with quercetin for wound healing applications using the ionic gelation method. In our study, we included quercetin in a blend of chitosan and hyaluronic acid based polymers. There are several other examples of the use of polymers and polymer blends as carriers of active ingredients for cosmetic applications. In the study by Esposito et al. [48], sodium alginate and poly(vinyl alcohol) hydrogels were proposed to enhance the transdermal delivery of quercetin. Supramolecular hydrogels based on poly(vinyl alcohol) containing quercetin for the elimination of bacteria and fungi were proposed by Kopka et al. [49]. Bharathi et al. synthesized and characterized poly-D-L-lactide (PLA) nanoparticles for the delivery of quercetin [50]. Quercetin was also incorporated into collagen/chitosan/SiO_2 composite to produce antioxidant biomaterials [51]. New fibrous materials based on the cellulose derivative and poly(ethylene glycol) containing quercetin were proposed by Stoyanov et al. using the electrospinning technique [52]. Quercetin was also used in starch-based films and its release was studied [53]. A considerable number of different configurations of polymer-based systems have been described in detail in the literature, including micelles, carriers, core-shell structures, nanospheres, hydrogels, membranes, and films [55-57]. A comprehensive review paper described by Wadhwa K. et al. includes a review of various nanoformulations containing quercetin dedicated to the local release of quercetin. The authors present the results obtained using, among others, nanocapsules, nanogels, and solid lipid nanoparticles, which are intended to affect the solubility and permeability of quercetin. Additionally, it was observed that nanocarriers affect the controlled release of the flavonoid to the dermal layer [57]. In the available literature, we did not find any manuscript describing the release of quercetin from chitosan films or chitosan films with added hyaluronic acid. Based on the literature review and our experimental results, we can conclude that quercetin-containing polymeric materials are promising candidates not only for cosmetic but also for biomedical and pharmaceutical applications. Mechanical properties of the polymeric film have not been studied in this study, but from our previous study, we believe that the mechanical properties are sufficient for cosmetic applications [24,40].

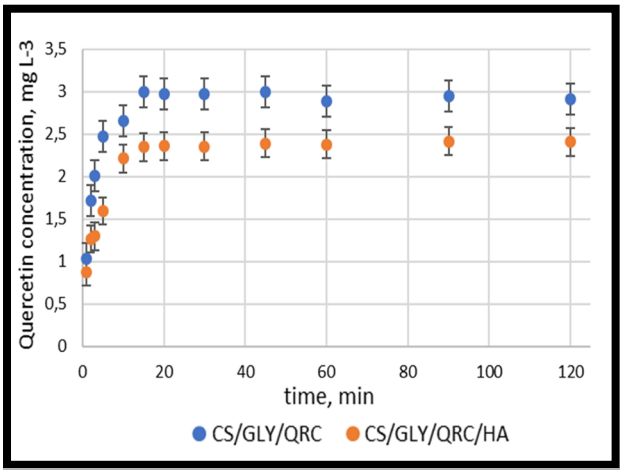

FIG. 6. The release of QRC from CS/GLY/QRC and CS/GLY/QRC/HA film.

Conclusions

For active delivery of quercetin for cosmetic purposes, we proposed chitosan-quercetin and chitosan-hyaluronic acid-quercetin films as an anti-ageing and beautifying cosmetic mask. The chitosan mask containing quercetin and glycerol has modified thermal properties. Chitosan films with glycerol were more thermally stable than chitosan films containing glycerol, hyaluronic acid, and quercetin. The addition of quercetin led to an increase in the surface roughness of the chitosan-based films. It is likely that the roughness of the resulting films will have a positive effect on the better contact between quercetin and the skin and therefore the better absorption of the compound into the skin. Examination of the release of quercetin from the obtained films indicated that maximum release of quercetin was observed after 20 minutes at pH 5.5. The average percentage release was higher for chitosan films than for chitosan/hyaluronic acid films.

Acknowledgements

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References

[1] Chen Q., Yang Z., Liu H., Man J., Oladejo A.O., Ibrahim S., Wang S., Hao B.: Novel drug delivery systems: An important direction for drug innovation. Research and development. Pharmaceutics 16 (2024) 674.
[2] Veeresham C.: Natural products derived from plants as a source of drugs. J. Adv. Pharm. Technol. Res. 3 (2012) 200-201.
[3] Fowler J.F. Jr., Woolery-Lloyd H., Waldorf H., Saini R.: Innovations in natural ingredients and their use in skin care. J. Drugs Dermatol. 9 (2010) S72–S81.
[4] Bowe W.P.: Advances in natural ingredients and their use in skin care. J. Drugs Dermatol. 12 (2013) 122-127.
[5] Kottner J., Lichterfeld A., Blume-Peytavi U.: Maintaining skin integrity in the aged: a systematic review. Br. J. Dermatol. 169 (2013) 528–535.
[6] De Lima Cherubim D.J., Buzanello Martins C.V., Oliveira Fariña L., da Silva de Lucca R.A.: Polyphenols as natural antioxidants in cosmetics applications. J. Cosmet. Dermatol. 19 (2020) 33–39.
[7] Silva S., Ferreira M., Oliveira A.S., Magalhaes C., Sousa M.E., Pinto M., Sousa Lobo J.M., Almeida I.F.: Evolution of the use of antioxidants in anti-ageing cosmetics. Int. J. Cosmet. Sci. 41 (2019) 378–386.
[8] Anand D.A., Arulmoli R., Parasuraman S.: Overviews of biological importance of quercetin: a bioactive flavonoid. Pharm. Rev. 10 (2016) 84-89.
[9] Jia E., Yan Y., Zhou M., Li X., Jiang G., Liu W., Zhang D.: Combined effects of dietary quercetin and resveratrol on growth performance, antioxidant capability and innate immunity of blunt snout bream (Megalobrama amblycephala). Anim. Feed Sci. Technol. 256 (2019) 114268.
[10] Xu D., Hu M.-J., Wang Y.-Q., Cui Y.-L.: Antioxidant activities of quercetin and its complexes for medicinal application. Molecules 24 (2019) 1123.
[11] Boesch-Saadatmandi C., Loboda A., Wagner A.E., Stachurska A., Jozkowicz A., Dulak J., Döring F., Wolffram S., Rimbach G.: Effect of quercetin and its metabolites isorhamnetin and quercetin-3--glucuronide on inflammatory gene expression. Role of miR-155. J. Nutr. Biochem. 22 (2011) 293-299.
[12] Dabeek W.M., Marra M.V.: Dietary quercetin and kaempferol. Bioavailability and potential cardiovascular-related bioactivity in humans. Nutrients 11 (2019) 2288.
[13] Kukongviriyapan U., Sompamit K., Pannangpetch P., Kukongviriyapan V., Donpunha W.: Preventive and therapeutic effects of quercetin on lipopolysaccharide-induced oxidative stress and vascular dysfunction in mice. Can. J. Physiol. Pharmacol. 90 (2012) 1345-1353.
[14] Ganceviciene R., Liakou A.I., Theodoridis A., Makrantonaki E., Zouboulis C.C.: Skin anti-aging strategies. Dermatoendocrinol. 4 (2012) 308-319.

[15] Kaşıkc M.B., Bağdatlıoğlu N.: Bioavailability of quercetin. Curr. Res. Nutr. Food Sci. J. 4 (2016) 146–151.
[16] Li A.-N., Li S., Zhang Y.-J., Xu X.-R., Chen Y.-M., Li H.-B.: Resources and biological activities of natural polyphenols. Nutrients 6 (2014) 6020-6047.
[17] Ribeiro A.S., Estanqueiro M., Oliveira M.B., Lobo J.M.S.: Main benefits and applicability of plant extracts in skin care products. Cosmetics 2 (2015) 48-65.
[18] Monteiro Â., Colomban S., Azinheira H.G., Guerra-Guimarães L., Silva M.D.C., Navarini L., Resmini M.: Dietary antioxidants in coffee leaves: impact of botanical origin and maturity on chlorogenic acids and xanthones. Antioxidants 9 (2019) 6.
[19] Dos Santos É.M., de Macedo L.M., Tundisi L.L., Ataide J.A., Camargo G.A., Alves R.C., Oliveira M.B., Mazzola P.G.: Coffee by-products in topical formulations: a review. Trends Food Sci. Technol. 111 (2021) 280-291.
[20] Wang X., Gong X., Zhang H., Zhu W., Jiang Z., Shi Y., Li L.: In vitro anti-aging activities of ginkgo biloba leaf extract and its chemical constituents. Food Sci. Technol. 40 (2020) 476-483.
[21] Soto M.L., Falqué E., Domínguez J.: Relevance of natural phenolics from grape and derivative products in the formulation of cosmetics. Cosmetics 2 (2015) 259-276.
[22] Brandt F.S., Cazzaniga A., Hann M.: Cosmeceuticals: Current trends and market analysis. Semin. Cutan. Med. Surg. 30 (2011) 141-143.
[23] Baell J.B.: Feeling Nature's PAINS: Natural Products, Natural Product Drugs, and Pan Assay Interference Compounds (PAINS). J. Nat. Prod. 79 (2016) 616-628.
[24] Kulka K., Sionkowska A.: Chitosan based materials in cosmetic applications: A review. Molecules 28 (2023) 1817.
[25] Casadidio C., Peregrina D.V., Gigliobianco M.R., Deng S., Censi R., Di Martino P.: Chitin and Chitosans: Characteristics, eco-friendly processes, and applications in cosmetic science. Mar. Drugs 17 (2019) 369.
[26] Aranaz I., Acosta N., Civera C., Elorza B., Mingo J., Castro C., de los Gandía M.L., Caballero A.H.: Cosmetics and cosmeceutical applications of chitin, chitosan and their derivatives. Polymers 10 (2018) 213.
[27] Menezes J., dos Santos H., Ferreira M., Magalhães F., da Silva D., Bandeira P., Saraiva G., Pessoa O., Ricardo N., Cruz B., et al.: Preparation, structural and spectroscopic characterization of chitosan membranes containing allantoin. J. Mol. Struct. 1199 (2020) 126968.
[28] Afonso C., Hirano R., Gaspar A., Chagas E., Carvalho R., Silva F., Leonardi G., Lopes P., Silva C., Yoshida C.: Biodegradable antioxidant chitosan films useful as an anti-aging skin mask. Int. J. Biol. Macromol. 132 (2019) 1262-1273.
[29] Yuan G., Chen X., Li D.: Chitosan films and coatings containing essential oils: The antioxidant and antimicrobial activity, and application in food systems. Food Res. Int. 89 (2016) 117-128.
[30] Ke C.-L., Deng F.-S., Chuang C.-Y., Lin C.-H.: Antimicrobial actions and applications of chitosan. Polymers 13 (2021) 904.
[31] Costa E.M., Silva S., Pina C., Tavaria F.K., Pintado M.M.: Evaluation and insights into chitosan antimicrobial activity against anaerobic oral pathogens. Anaerobe 18 (2012) 305–309.
[32] Jangra N., Singla A., Puri V., Dheer D., Chopra H., Malik T., Sharma A.: Herbal bioactive-loaded biopolymeric formulations for wound healing applications. RSC Advances 15 (2025) 12402-12442.
[33] Udaya Rajesh R., Dhanaraj S.: Therapeutic potentials and targeting strategies of quercetin on cancer cells: Challenges and future prospects. Phytomedicine 133 (2024) 155902.
[34] Kurniawan M.F., Setyawan D., Hariyadi D.M.: Quercetin in drug carriers: Polymer composite, physical characteristics, and in vitro study. Science and Technology Indonesia 9 (2024) 380-412.
[35] Diez-Echave P., Ruiz-Malagón A.J., Molina-Tijeras J.A., Hidalgo-García L., Vezza T., Cenis-Cifuentes L., Rodríguez-Sojo M.J., Cenis J.L., Rodríguez-Cabezas M.E., Rodríguez-Nogales A., et al.: Silk fibroin nanoparticles enhance quercetin immunomodulatory properties in DSS-induced mouse colitis. Int. J. Pharm. 606 (2021) 120935.
[36] Heneczkowski M., Kopacz M., Nowak D., Kuźniar A.: Infrared spectrum analysis. Acta Pol. Pharm. 58 (2001) 415-420.
[37] Melro E., Antunes F.E., da Silva G.J., Cruz I., Ramos P.E., Carvalho F., Alves I.: Chitosan films in food applications. Tuning film properties by changing acidic dissolution conditions. Polymers 13 (2021) 1.
[38] Mahmoud A.A., Osman O., Eid K., Ashkar E.A., Okasha A., Atta D., Eid M., Aziz Z.A., Fakhry A.: FTIR spectroscopy of natural bio-polymers blends. Middle East J. Appl. Sci., 4 (2014) 516.
[39] Kim K.M., Son J.H.S., Kim S.-K.: Properties of chitosan films as a function of pH and solvent type. J. Food Sci. 71 (2006) 119-124.
[40] Sionkowska A., Kaczmarek B., Michalska M., Lewandowska K., Grabska S.: Preparation and characterization of collagen/chitosan/hyaluronic acid thin films for application in hair care cosmetics. Pure Appl. Chem. 89 (2017) 1829-1839.
[41] Lewandowska K., Sionkowska A., Grabska S., Kaczmarek B., Michalska M.: The miscibility of collagen/hyaluronic acid/chitosan blends investigated in dilute solutions and solids. J. Mol. Liq. 220 (2016) 726-730.
[42] Feng Z., Zheng Y., Zhao L., Zhang Z., Sun Y., Qiao K., Xie Y., Wang Y., He W.: An ultrasound-controllable release system based on waterborne polyurethane/chitosan membrane for implantable enhanced anticancer therapy. Mater. Sci. Eng. C 104 (2019) 109944.
[43] Lopes L., Molina E., Chiavacci L., Santilli C.V., Briois V., Pulcinelli S.H.: Drug-matrix interaction of sodium diclofenac incorporated into ureasil-poly(ethylene oxide) hybrid materials. RSC Adv. 2 (2012) 5629–5636.
[44] Choi M.-H., Shin H.-J.: Anti-melanogenesis effect of quercetin. Cosmetics 3 (2016) 18.
[45] Arung E.T., Furuta S., Ishikawa H., Kusuma I.W., Shimizu K., Kondo R.: Anti-melanogenesis properties of quercetin- and its derivative-rich extract from Allium cepa. Food Chem. 124 (2011) 1024-1028.
[46] Saija A., Tomaino A., Trombetta D., Pellegrino M.L., Tita B., Messina C., Bonina F.P., Rocco C., Nicolosi G., Castelli F.: 'In vitro' antioxidant and photoprotective properties and interaction with model membranes of three new quercetin esters. Eur. J. Pharm. Biopharm. 56 (2003) 167-174.
[47] Choudhary A., Vinay Kant V., Jangir B.L., Joshi V.G.: Quercetin loaded chitosan tripolyphosphate nanoparticles accelerated cutaneous wound healing in Wistar rats. Eur. J. Pharmacol. 880 (2020) 173172.
[48] Esposito L., Barbosa A.I., Moniz T., Lima S.C., Costa P., Celia C., Reis S.: Design and characterization of sodium alginate and poly(vinyl) alcohol hydrogels for enhanced skin delivery of quercetin. Pharmaceutics 12 (2020) 1149.
[49] Kopka B., Kost B., Wrześniewska J., Rajkowska K., Kadłubowski S., Kunicka-Styczyńska A., Baryga A., Gonciarz W., Basko M., Brzeziński M.: Supramolecular poly(vinyl alcohol)-based hydrogels containing quercetin for bacterial and fungal elimination. Eur. Polym. J. 187 (2023) 1-9.
[50] Sambandam B., Kumar S., Ayyaswamy A., Yadav N., Thiyagarajan D.: Synthesis and characterization of poly D-L lactide (PLA) nanoparticles for the delivery of quercetin. Int. J. Pharm. Pharm. Sci. 7 (2015) 42–49.
[51] Le T.H., Nguyen T.H.C., Tran T.V.T., Le L.S., Ho X.A.V., Tran T.M., Le Q.V.: Quercetin-incorporated collagen/chitosan/SiO_2 composite toward the robust antioxidant biomaterials. Int. J. Polym. Mat. Polym. Biomat. 73 (2023) 1-8.
[52] Stoyanova N., Spasova M., Manolova N., Rashkov I., Georgieva A., Toshkova R.: Antioxidant and antitumor activities of novel quercetin-loaded electrospun cellulose acetate/polyethylene glycol fibrous materials. Antioxidants 9 (2020) 232.
[53] Farrag Y., Ide W., Montero B., Rico M., Rodríguez-Llamazares S., Barral L., Bouza B.: Starch films loaded with donut shaped starch--quercetin microparticles: Characterization and release kinetics. Int. J. Biol. Macromol. 118 (2018) 2201-2207.
[54] Tomou E.-M., Papakyriakopoulou P., Saitani E.-M., Valsami G., Pippa N., Skaltsa H.: Recent advances in nanoformulations for quercetin. Pharmaceutics 15 (2023) 1656.
[55] Mandić L., Matković M., Baranović G., Šegota S.: The increased release kinetics of quercetin from superparamagnetic nanocarriers in dialysis. Antioxidants 12 (2023) 732.
[56] Wadha K., Kardian V., Puri V., Yogeshvar B., Sharma A., Pahwa R., Rao R., Gupta M., Singh I.: New insights into quercetin nanoformulations for topical delivery. Phytomedicine Plus 2 (2022) 100257.
[57] Lewandowska K., Sionkowska A., Kurzawa M.: Physical properties and release profiles of chitosan mixture films containing salicin, glycerin and hyaluronic acid. Molecules 28 (2023) 7827.