RELEASE OF APPLE EXTRACT AND PHENOLIC COMPOUNDS FROM FIVE SEMI-SOLID FORMULATIONS

Abstract. The clinical effectiveness of the phenolic compounds from apple extract will depend not only on their activity potency but also on the achieve of their action targets, and to achieve local biological effect from designed topical formulations, active substances have to be released from it. The aim of our study was to perform release test in vitro of emulsion, emulgel, gel, ointment, and oleogel containing an apple extract and individual phenolic compounds solutions. The release of phenolic compounds from semi-solid forms was assessed by Franz-type diffusion cells. The phenolic compounds of apple extract, and pure individual phenolic compounds released from five different semi-solid formulations results arrange in the following order: oleogel< ointment< gel< emulgel< emulsion. The in vitro release test showed that after 6 hours analysis the highest amount (70.6%) of phenolic compounds was released from emulsion, the lowest contents 31.6% and 29.2% were released from ointment and oleogel, accordingly. We found, that chlorogenic acid was the predominant phenolic compound released from the five different semi-solid forms after 1–6 hours. The physicochemical properties of the investigated semi-solid formulations might have influenced the content of phenolic compounds released.

Keywords: antioxidants; apples; topical; release

Introduction

Phenolic compounds are one of the main biological active compounds
determined of plants with antioxidant activities [1]. Apple is one of the most cultivated fruits in the world with high nutritional value, which predetermined of phenolic compounds [2,3]. Phenolic compounds with anti-inflammatory, antioxidant, antibacterial, antiviral, antifungal, anticancer, immune system-promoting activities are important in the treatment of skin disorders. Various of phenolic groups compounds protect skin from UV radiation, slows down premature aging, and hyper-pigmentation [4,5]. Consequently, due to their multifaceted biological activities, the phenolic compounds determined in apples are an interesting candidate for the development of topical formulations for pharmaceutical and medical application.

The clinical effectiveness of the phenolic compounds will depend not only on their activity potency but also on the achieve of their action targets [6,7]. Consequently, it is relevant to select potent phenolic compounds that have high skin absorption and target accessibility. On the side, there is a need for the development of techniques to enhance the delivery and efficacy of selected. The selection of the suitable delivery system depends on many factors, such as the hydrophobicity or hydrophilicity of the active agents, the route of transport into the body, and the preferred release profile of the substances [8]. One of the relevant stages in order to receive therapeutic response of biological active compounds is the selection of the suitable pharmaceutical forms. In our research, semi-solid pharmaceutical forms emulsion, emulgel, gel, ointment, and oleogel – were selected. Emulgels are simply emulsions which are gelled by mixing them with a gelling material. In an emulsion, the entrapped active substance is slowly released from the internal phase through the external phase and slowly gets absorbed through the skin [9]. Further, gels and emulgels have excellent properties such as being thixotropic and readily detachable, spreading readily, being non-oily, negotiating with numerous excipients, and being non-staining, miscible, transparent, and biofriendly [10]. Meanwhile, ointments have some limitations such as a lower spreading coefficient, less penetration through the Stratum Corneum, and less patient compliance due to stickiness or need to apply with rubbing [10].

To achieve local biological effect from designed topical formulations, active substances have to be released from it. The release of phenolic compounds and
further skin penetration depends on the form, free aglycone or glycoside, molecular weight, stability, solubility, and bioavailability [11-13]. Phenolic compounds glycoside forms are characterized by better solubility in water and thus higher hydrophilicity as compared to aglycone forms. However, due to their high molecular weight and a lower lipophilicity, skin bioavailability of phenolic glycosides is lower compared to aglycone forms of these compounds [14,15]. A part of the complex process of penetration into the skin layers is the release of active compounds from the delivery systems. The increasing the release rate of the substances from the topical formulations, could improve percutaneous absorption and thus induce faster reach the skin and finally to overcome the Stratum Corneum barrier and penetrate into deeper skin layers [16,17]. The release rates of active substances from semi-solid formulations depend directly on the physiochemical properties of the delivery system and the active substance properties.

The aim of our study was to perform release test in vitro of emulsion, emulgel, gel, ointment, and oleogel containing an apple extract and individual phenolic compounds solutions.

Materials and Methods

In this study, we used apple extract of ‘Kostele’ apple cultivar, and solution of purified individual phenolic compounds (chlorogenic acid, rutin, quercetin, (+)-catechin, and (−)epicatechin) standards. The determination of the release of phenolic compounds from emulsion, emulgel, gel, ointment, and oleogel formulations was performed using Franz-type diffusion cells with natural cellulose dialysis membranes. The receptor compartment contained an ethanol-water mixture at the ratio of 1:1, the temperature being 37.0 ± 0.5 °C. The donor compartment contained 1.0 g of experimental formulations. A dialysis tubing cellulose membrane was placed between the donor and the receptor compartments. The receptor medium was stirred using the hotplate magnetic stirrer [18]. The 1.0 mL samples of the acceptor medium were taken after 1 h, 2 h, 3 h, 4 h, and 5 h, and the last samples were taken after 6 h. The samples were analyzed by applying the HPLC-PDA method.

Results

In vitro release test of phenolic compounds of apple extracts from five semi-
solid formulations was performed and showed, that in 1–6 hours the highest total content of phenolic compounds released from emulsion. The test showed that the largest amounts 70.6% of total phenolic compounds was released from emulsion after 6 hours. The lowest levels 31.6% and 29.2% of total phenolic compounds were released from ointment and oleogel after 6 hours, accordingly. Mixture of pure individual phenolic compounds (chlorogenic acid, rutin, quercetin, (+)-catechin, and (-)-epicatechin) release profile from five semi-solid forms was accomplished. *In vitro* release test showed, that in 1–6 hours the largest content of individual phenolic compounds was released from emulsion also. The highest amount 74.6% of individual phenolic compounds was released from emulsion after 6 hours, while the smallest amounts 45.8% and 43.2% were released from ointment and oleogel formulations, respectively. *In vitro* release test showed, that only chlorogenic acid, rutin, and quercetin were released from experimental formulations. Meanwhile, the (+)-catechin and (-)-epicatechin was not released from five different semi-solid forms after 6 hours. From the pure individual phenolic compounds released after 6 hours, the percentage released from formulations was established. We found, that chlorogenic acid was the predominant phenolic compound released from the five different semi-solid forms after 1–6 hours. The comparison of the contents of individual phenolic compounds released from the test formulations showed, that the largest amounts of chlorogenic acid was released from emulsion (85.9%). Ointment and oleogel formulations were released the lowest amounts of chlorogenic acid (36.2% and 33.4%, respectively). Emulgel and gel formulations were released average contents of the chlorogenic acid (75.0% and 66.1%, accordingly). *In vitro* release test showed, that the maximum levels of rutin was released from emulsion (71.9%). Emulgel and gel formulations were released average levels of the rutin (59.1% and 57.8%, accordingly). Ointment and oleogel formulations were released the smallest amounts of rutin (34.8% and 31.9%, respectively). Unlike the previously described research results, the largest amounts of quercetin were released from emulgel (79.1%). From ointment and oleogel formulations were released the higher amounts of quercetin compared with released contents of chlorogenic acid and rutin. Ointment, oleogel, and emulsion formulations were released the lowest
amounts of quercetin (66.5%, 64.5%, and 65.9%, accordingly). Gel formulation was released average contents of the quercetin (74.6%). Regarding in vitro release studies, the better release results of phenolic compounds may be explained on the basis of difference in viscosity between semi-solid forms. One of the reasons why the highest content of phenolic compounds was release from emulsion could be an accelerated diffusion due to the lower viscosity of the emulsions [16]. The lowest released profiles of phenolic compounds from ointment and oleogel may be influenced by high viscosity of hydrophobic base which reduces the rate of the diffusion of the active agents within the formulation and thus their release [19].

Conclusions

The phenolic compounds of apple extract, and pure individual phenolic compounds released from five different semi-solid formulations results arrange in the following order: oleogel< ointment< gel< emulgel< emulsion. We found, that chlorogenic acid was the predominant phenolic compound released from the five different semi-solid forms after 1–6 hours. The physicochemical properties of the investigated semi-solid formulations might have influenced the content of phenolic compounds released as well as the release kinetics.

References:


