REPROCESSING WASTE MATERIALS TO PRODUCE FILM-FORMING POLYMERS FOR PHARMACEUTICAL ORAL FILMS – REVIEW

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Growing demands for environmental sustainability and responsible exploitation of natural resources has led to increased research on the potential use and reprocessing of different waste materials as primary source of starting materials for different industries. Rigorous quality requirements for pharmaceutical active and auxiliary substances is hindering wider use of reprocessed waste materials in pharmaceutical industry. However, certain advances have been recently introduced in the field of natural polymers (biopolymers) production (1).

Biocompatible, biodegradable and, generally, non-toxic biopolymers offer numerous advantages in different drug delivery systems development. In this review, focus is on biopolymers used as potential film-forming agents (FFA) for pharmaceutical oral films. An overview of the most commonly used biopolymers produced from different waste materials, resources used, and their application in pharmaceutical oral films manufacture is schematically presented in Figure 1.

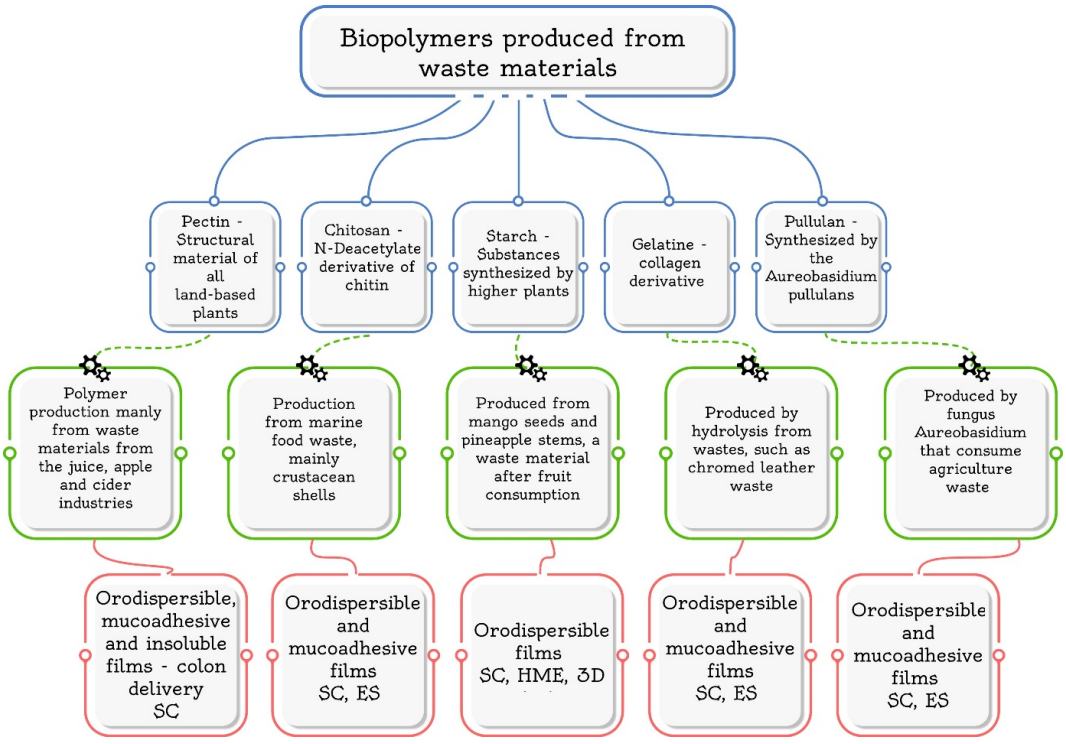

Figure 1. Biopolymers obtained from waste materials, their potential usage for oral film development, and manufacturing methods employed (SC – solvent casting; ES – electrospinning; HME – hot-melt extrusion; 3D – three-dimensional printing)

Pullulan is employed in relatively low concentrations as FFA in pharmaceutical oral films, it is soluble in hot water, and prepared films exhibit fast hydration and swelling in contact with aqueous media. It is perceived as valuable eco-friendly FFA since high amounts of pullulan can be produced by fungus *Aureobasidium pullulans* which consume agricultural waste. Starch, synthesized by higher plants, and modified starches are broadly applied in different industries. Since starch demands are high, it requires large-scale industrial production, so possibility for its production by waste reprocessing would be advantageous. Pregelatinized starch is more commonly used for oral films as it can be dispersed in cold water (up to 30%), rapidly swells in contact with medium and shows excellent wettability (1, 2). Pectin is water-soluble polymer, present as structural material in cell-wall of different plants. It is not yet widely explored for oral film development. Useful concentration range for this polymer is narrow (around 3%) and, consequently, it is challenging to prepare films with desired characteristics. Gelatin is predominantly found in connective tissues, porcine and bovine skin, but may also be obtained from marine sources. Gelatin-based films are highly mucoadhesive independently of its concentration (usually around 2%), but wettability is poor. It is noted that film properties, manly its disintegration behavior may depend on the gelatin source (3).

With the attention drawn to environmental sustainability, natural excipients are becoming highly regarded, especially those that can be produced from existing agricultural and industrial waste. Based on their favourable characteristics, it is expected that polymers obtained from reprocessed waste materials will gain increased role in pharmaceutical oral films development.

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2. Bodini R, Guimarães J, Monaco-Lourenço C, Aparecida de Carvalho R. Effect of starch and hydroxypropyl methylcellulose polymers on the properties of orally disintegrating films. J Drug Deliv Sci Technol. 2019;51: 403-410.
3. Kwak H, Woo H, Kim I, Lee K. Fish gelatin nanofibers prevent drug crystallization and enable ultrafast delivery. RSC Advanc. 2017;7(64): 40411-40417.

Acknowledgement

This research was funded by the Ministry of Education, Science and Technological Development, Republic of Serbia, through Grant Agreement with the University of Belgrade - Faculty of Pharmacy No: 451-03-68/2020-14/200161

PREGLED POLIMERA ZA IZRADU FARMACEUTSKIH ORALNIH FILMOVA DOBIJENIH PRERADOM RAZLIČITIH OTPADNIH MATERIJALA

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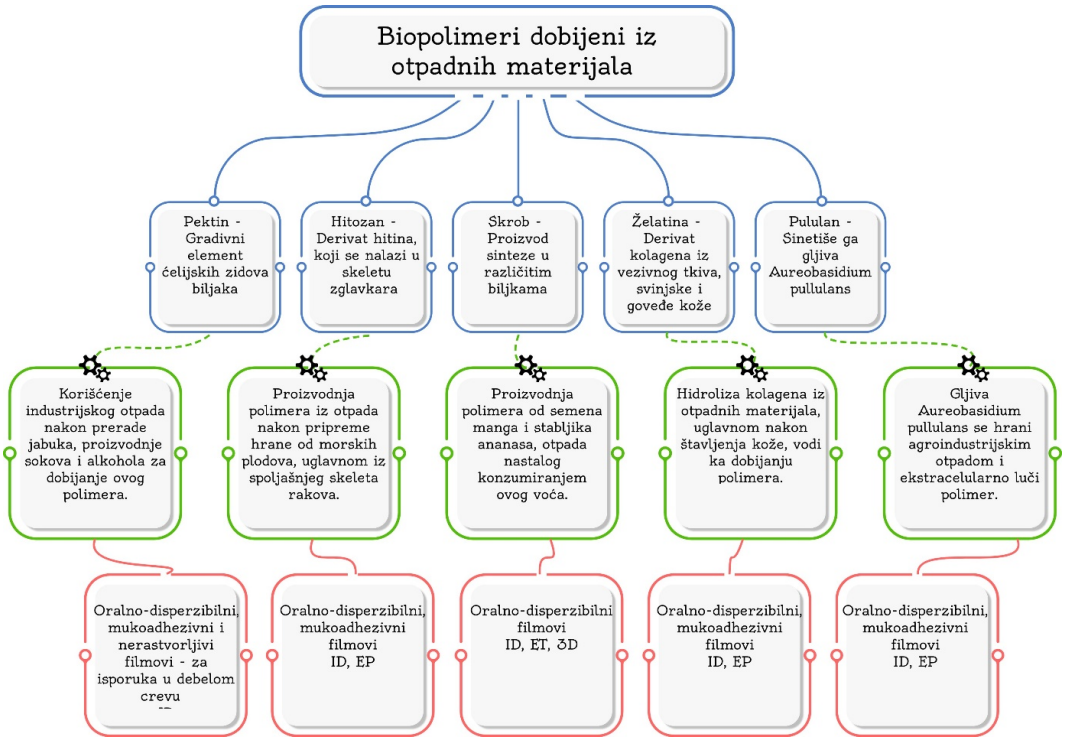
Održiva životna sredina i odgovorno korišćenje prirodnih resursa postali su značajan zadatak za moderno društvo, što je dovelo do povećanja aktivnosti na polju istraživanja o mogućnosti korišćenja i obradi različitih otpadnih materijala kao primarnog izvora polaznih supstanci za različite grane industrije. Rigorozni zahtevi za kvalitet aktivnih i pomoćnih supstanci ograničavaju širu upotrebu prerađenih materijala u farmaceutskoj industriji. Ipak, određeni pomaci postoje na polju dobijanja prirodnih polimera (biopolimera) (1). Biokompatibilni, biorazgradivi i netoksični biopolimeri nude brojne prednosti. Ovaj pregled usmeren je na biopolimere koji potencijalno mogu da se koriste kao sredstva za formiranje filma prilikom razvoja oralnih filmova kao farmaceutskog oblika leka. Pregled najčešće korišćenih biopolimera koji se proizvode iz različitih otpadnih materijala, korišćeni izvori za proizvodnju i njihova primena u izradi farmaceutskih oralnih filmova je shematski prikazana na Slici 1.



Slika 2. Pregled biopolimera dobijenih iz otpadnih materijala, njihova potencijalna primena za izradu oralnih filmova i metode izrade koje se koriste (ID –izlivanje disperzije; EP – elektropredenje; ET – ekstruzija topljenjem; 3D – trodimenzionalno štampanje)

Pululan se, kao polimer za farmaceutske oralne filmove, koristi u relativno niskim koncentracijama, rastvorljiv je u vreloj vodi, a pripremljeni filmovi brzo upijaju vodu i bubre u kontaktu sa medijumom. Smatra se ekološki prihvatljivim, s obzirom da gljiva *Aureobasidium pullulans*, koja se hrani agroindustrijskim otpadom, ima sposobnost proizvodnje većih količina pululana. Skrob, proizvod sinteze u biljkama, i modifikovani skrobovi se široko koriste u različitim industrijama. Potrebe za skrobom su velike i proizvodnja se odvija u velikim industrijskim pogonima, pa bi mogućnost proizvodnje skroba iz otpadnih materijala bila ekološki veoma značajna. Pregelirani skrobovi se češće koriste za izradu oralnih filmova s obzirom da se mogu rastvoriti u hladnoj vodi (u koncentraciji do 30%), brzo bubre u kontaktu sa medijumom i pokazuju odličnu sposobnost kvašenja (1, 2). Pektin predstavlja gradivni element zidova biljaka i rastvorljiv je u vodi. Još uvek nije široko zastupljen u izradi oralnih filmova. Raspon pogodnih koncentracija pektina je uzak (oko 3%) i posledično je zahtevno pripremiti filmove željenih karakteristika. Želatina se pretežno nalazi u vezivnom tkivu, goveđoj i svinjskoj koži, ali određene količine su prisutne i u morskim organizmima. Filmovi izrađeni od želatine su mukoadhezivni nezavisno od koncentracije (uobičajena koncentracija je 2%), ali je sposobnost kvašenja loša. Uočeno je da karakteristike filmova, posebno njihova raspadljivost, zavise od toga iz kog izvora je želatina dobijena (3).

Održivost životne sredine privlači veliku pažnju, pa su biopolimeri postali izuzetno značajni kao polazne supstance, posebno kada se mogu dobiti preradom agroindustrijskog otpada. Imajući u vidu pogodne farmaceutsko-tehnološke karakteristike biopolimera dobijenih preradom različitih otpadnih materijala, može se očekivati da će njihova primena zauzeti značajno mesto u razvoju i proizvodnji farmaceutskih oralnih filmova.

Literatura

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Zahvalnica

Ovo istraživanje finansirano je od strane Ministarstva prosvete, nauke i tehnološkog razvoja Republike Srbije kroz Ugovor o saradnji sa Univerzitetom u Beogradu - Farmaceutskim fakultetom broj 451-03-9 / 2021-14 / 200161.