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Rosin: A naturally derived excipient in drug delivery systems

Kalafonia: naturalnie uzyskiwana substancja pomocnicza w systemach dostarczania leku

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Summary

Natural polymers are primarily attractive because they are biodegradable, inexpensive, and readily available. The most important benefit of natural polymers is that they are capable for chemical modifications. One such biopolymer, rosin, and its derivatives have been pharmaceutically evaluated as microencapsulating materials, film forming agent and as binding agent in formulation of tablets. They are also employed in formulation of chewing gum bases and cosmetics. This review article provides an overview of pharmaceutical use of rosin and its derivatives as excipient in dosage forms as well as novel drug delivery systems (**Polim. Med. 2013, 43, 1, 45–48**).

Key words: rosin, biodegradable, drug delivery, controlled release, sustained release, film forming agent

Streszczenie

Naturalne polimery ulegają biodegradacji, są tanie i łatwo dostępne. Najistotniejszą korzyścią zastosowania naturalnych polimerów jest ich zdolność do poddawania się chemicznym modyfikacjom. Jednym z takich biopolimerów jest kalafonia oraz jej pochodne, które były oceniane farmaceutycznie jako materiały w mikrokapsułkowaniu, środki tworzące błonę oraz środki wiążące w preparatach tabletkowych. Są one również stosowane w formowaniu gumy do żucia i kosmetyków. W artykule przedstawiono przegląd farmaceutycznego wykorzystania kalafonii i jej pochodnych jako substancji pomocniczych w formach dawkowania oraz systemach dostarczania leków (**Polim. Med. 2013, 43, 1, 45–48**).

Słowa kluczowe: kalafonia, podaż leku, kontrolowane uwalnianie, przedłużone uwalnianie, środek tworzący błonę

Introduction

In last decades, numerous natural gums have been investigated as polymers for designing and development of pharmaceutical dosage forms. The employment of natural polymers and mucilage in sustained and controlled drug delivery systems continues to be a field of research [1–3].

Rosin is a clear or semi-transparent solid. It is pale yellow to dark amber thermoplastic solid. It occurs naturally in oleoresins of pine tree (*Pinus soxburghi* and *Pinus toeda*, family *Pinaceae*). It is also known as colophony. It is obtained by heating fresh liquid resin of tree. The most important property which makes its utilization is that, at room temperature rosin exists as brittle material and on heating it melts. In the field of drug delivery, the excellent film-forming property of rosin is generally utilized.

The other benefits of rosin include its biodegradation and biocompatibility characteristics which increased its applicability. It is soluble in organic solvents (ether, chloroform, and benzene). Abietic acid and pimaric acid are the main chemical constituents of rosin. It also comprises of a small amount of nonacidic materials [1].

Approximately, 90% rosin acids are present in rosin. Monocarboxylic acids are the rosin acids. It is reported in numerous studies that rosin and esters of rosin possesses good film forming capability. These esters are used for enteric coating in tablet dosage forms. Biodegradation rate of rosin, and compatibility between drug and rosin are the factors which govern the release of drug from rosin dosage form.

Polymerized rosin is light yellow in colour. Softening point of polymerized rosin is 75°C to 80°C. Polymerized rosin is formed by polymerization of abietic acid.

Polymerized rosin has excellent film-forming capability as compared to rosin. Dehydroabietic acid (rosin derivative) possesses anti-tumour activity. Rosin is also a good emulsifying agent.

Pharmaceutical applications of rosin

Rosin and its derivatives have been investigated for their utilization as film coating agent. These are also evaluated as matrix forming agent, and in microencapsulation. Rosin derivatives and its glycerol, sorbitol and mannitol esters are reported to have excellent film forming properties and can be used for enteric coating and delayed release of drug [1].

Fulzele et. al. (2002) characterized and investigated polymerized rosin as a novel film forming agent. They employed diclofenac sodium as model drug. The films were prepared by solvent evaporation method. Plasticizers such as tributyl citrate and dibutyl sebacate were used. Prepared films were characterized for % elongation, tensile strength, and water vapour transmission. Results of their study revealed that the release of drug from coated pellets was in sustained manner. From their study they concluded that polymerized rosin films plasticized with hydrophobic plasticizers could be used in coating processes for the design of oral sustained drug delivery dosage forms [4].

Nande et. al. (2008) studied the use of PEGylated derivatives of rosin as sustained release polymer and as a film forming materials. In their study they employed two PEGylated derivatives of rosin (derivative I and II). Two drugs diclofenac sodium and propranolol hydrochloride were used as model drugs. The prepared films were characterized for surface morphology (SEM), water vapor permeation rate, mechanical properties, and permeability study. The prepared films were found smooth and continuous. The mechanism of drug release from films systems followed zero order. They suggested that rosin derivatives retard the release of model drugs. Hence these derivatives provide an alternative to the conventionally used polymers [5].

Satturwar et. al. (2004) synthesized and evaluated the physicochemical properties of two new rosin derivatives. Films were prepared by solvent evaporation method. The films were evaluated for surface morphology, and water vapor permeation rate. The films were smooth and have uniform surface. The release of drug (diclofenac sodium) was sustained up to 10 hr. The results of study suggested that rosin derivatives could be used in design and development of films to prolong the drug release [6]. Satturwar et al (2002) synthesized rosin-based polymers and characterized for the coating properties. Films of diclofenac sodium with polymers were prepared by solvent evaporation method. Sus-

tained release of the drug was observed from coated pellets [7]. In another study, Suniket et al (2002) evaluated the film forming and coating properties of rosin derivatives. The derivatives were glycerol ester of maleic rosin and pentaerythritol ester of maleic rosin. The prepared films showed the sustained release of diclofenac sodium for up to 10 hours. From the obtained results they concluded the utilization of rosin-based biomaterials for sustained-release drug delivery systems [8].

In a study, hydrogenated rosin was investigated as film-coating material. Satturwar et. al. (2003), prepared films by employing hydrogenated rosin. The films were fabricated by casting method using dibutyl sebacate, as a hydrophobic plasticizer. The result showed the good film-coating property of hydrogenated rosin [9]. In spite of their excellent film-forming property, rosins have been scantily evaluated for transdermal drug delivery by Prashant et al (2005). Prashant et al (2005) evaluated polymerized rosin for its use in transdermal drug delivery systems. They suggested that polymerized rosin in combination with PVP leads smooth flexible films. The prepared film showed good tensile strength and percentage elongation. From the results they concluded that polymerized rosin could be used in the design of transdermal drug delivery system [10].

Rosin and rosin derivatives have been employed to prepare microcapsules and nanoparticles. Lee et. al. (2005) prepared hydrocortisone-loaded rosin nanoparticles. The nanoparticles were prepared by dispersion and dialysis method. The results of evaluation parameters showed that the prepared nanoparticles were spherical in shape and possessed 167–332 nm diameters. The drug loading in nanoparticles were approximately 50%. As the content of rosin increased, drug release gradually decreased from nanoparticles. From their study they suggested that nanoparticles based on rosin could be useful as a drug delivery system [11].

Sheorey et. al. (1991) prepared rosin microcapsules by a solvent evaporation technique. They evaluated the effect of solvent on release characteristics of microcapsules. In their study, they found that as the rate of evaporation of the solvent decreased, the mean diameter decreased and drug content increased. Slow evaporating solvents produced thin walled microcapsules [12].

Sustained release sulphadiazine microcapsules were prepared by employing rosin-glycerol ester. From the results it was concluded that sulphadiazine release followed first order kinetics [13]. In another study Sheorey et. al. (1994) prepared and studied the release kinetics of sulphadiazine rosin ester microcapsules. The prepared microcapsules were evaluated for size and *in vitro* drug release in simulated gastric and intestinal fluids [14].

Fulzele et. al. (2004) characterized polymerized rosin as a microcapsule wall forming substance. They prepared diclofenac sodium microcapsules by using polymerized rosin. They employed solvent evaporation formulation approach. The results showed drug release

kinetics for microcapsules followed Higuchi release pattern. Microcapsules showed drug release for upto 10 h in phosphate buffer (pH 7.4) [15]. In an attempt it was found that aspirin release was retarded by rosin and rosin derivatives. Aspirin matrix tablets were prepared using a wet granulation technique and characterized for hardness, disintegration time, and *in vitro* drug release. Hardness studies showed that all tablet possessed hardness above 6 kg/cm². All tablets showed disintegration time greater than 150 min. *In vitro* dissolution studies were carried out in phosphate buffer (pH 7.2). Tablet containing rosin showed first-order release profile. Tablet formulations showed controlled release of more than 4 h. Hence, rosin is a promising basis in design of controlled drug delivery system [16].

Satturwar et. al. (2003) evaluated the biodegradation and *in vivo* biocompatibility of rosin. They used both *in vitro* and *in vivo* methods for evaluation. They conducted *in vitro* degradation test by placing rosin film in phosphate buffered saline (pH 7.4) at 37°C for up to 3 months. For studying the biocompatibility poly (DL-lactic-co-glycolic acid) was used as reference. The results showed that films degraded in specific time. From their study they concluded that rosin could be used in transdermal drug delivery system [17]. Mandaogade et. al. (2002) evaluated rosin derivatives as polymers for controlled release film formulations. Diclofenac sodium film composed of rosin derivatives (RD-1 and RD-2) were prepared by solvent evaporation method. Film showed sustained release of more than 10 h. Hence,

rosin derivatives (RD-1 and RD-2) are promising basis in the design of controlled drug delivery system [18].

In a study microcapsules were also prepared by using abietic acid. Puranik et. al. (1992) isolated abietic acid from rosin. They used abietic acid as a wall-forming material. They evaluated prepared microcapsules for various parameters including their size, density, wall thickness and *in vitro* release characteristics in gastric fluid. They found that microcapsules showed sustained release of drug [19].

In 1990, Pathak et. al. evaluated the release kinetics of rosin hard paraffin combination (RHPC) coated aspirin microcapsules. They also studied the effect of pH on the drug release. Microcapsules were formulated by pan coating method. The results showed that coated microspheres were resistant to acidic pH. The release of drug was less than 5%. On the other hand in pH 7.2 the drug was quickly released. The drug release though coated microcapsules followed first order pattern [20].

Conclusion

It can be concluded that rosin and its derivative have good potential as pharmaceutical excipients. It could be used as a binding agent, coating and matrix forming agent in tablet formulations. It can also be utilized as microencapsulating agent. Various studies showed that rosin and rosin derivatives have capability to formulate sustained and controlled release drug system.

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