

ROSIN AN IMPORTANT POLYMER FOR DRUG DELIVERY: A SHORT REVIEW

Om Prakash Pal*, Rishabha Malviya, Vipin Bansal, Pramod Kumar Sharma

Department of Pharmaceutical Technology, Meerut Institute of Engineering and Technology, Baghpat Bypass, Delhi Roorki Highway, Meerut-250005, Uttar Pradesh, India

*Email: ompaul1111@gmail.com

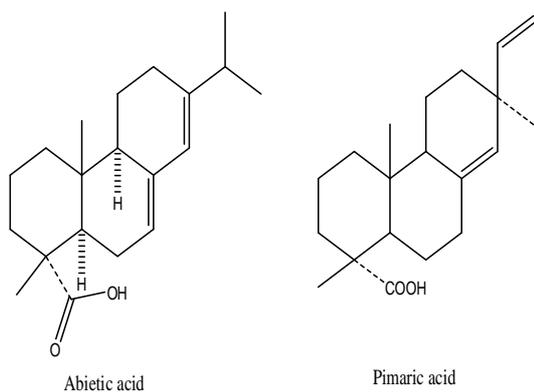
ABSTRACT

Natural polymers are widely used in pharmaceutical formulations. They are biodegradable and generally nontoxic in nature. In this review pharmaceutical application of rosin is characterized. Rosin is a natural non-volatile resinous mass obtained from *Pinus palustris*. Physico-chemical characteristics and ease of availability of rosin provide a platform to use it as a polymer for different drug delivery systems. It can be concluded from the article that this polymer may be used to formulate various controlled and targeted drug delivery system.

Keywords: Rosin, Drug delivery, *Pinus palustris*, Biodegradable, Natural polymer

INTRODUCTION

Various natural gums and mucilages have been examined as polymers for control and sustained drug release, in the last few decades^{1, 2}. Natural polymers remain attractive primarily because they are commercial, readily available, capable of multitude of chemical modifications and potentially degradable and compatible due to their origin. Biodegradable polymers have been used widely as drug delivery systems because of their biocompatibility and biodegradability. Biodegradable polymer particles (e.g., microspheres, microcapsules, and nanoparticles) are highly useful because they can be administered to a variety of locations *in-vivo* through a syringe needle^{3, 4}. Rosin is a natural non-volatile resinous mass obtained from *Pinus palustris* Miller and other species such as *Pinus linnae*. Some rosin biopolymers are reported to have excellent biocompatibility and biodegradation features⁵. It primarily contains resin tricyclic diterpene carboxylic acids (abietic and pimaric) and a few amounts of nonacidic components.



Rosin contains approximately 90% rosin acids. The rosin acids are monocarboxylic acids and have a typical molecular formula $C_{20}H_{30}O_2$. The prominent ones include abietic acid with conjugated double bonds and pimaric acid with non-conjugated double bonds. The rosin acid molecules possess two chemically reactive centres, the double bonds and the carboxyl group. Rosin and its derivatives are widely used in paints, varnishes, cosmetics, printing inks, and chewing gums. The importance

traditional applications of rosin and its derivatives includes, as paper sizing agents, adhesives, printing inks and chewing gum has declined due to escalating production labour costs. However rosin remains an attractive renewable source of chemicals useful for polymer synthesis or in the pharmaceutical industry.

Esters of rosin are reported to have good film forming properties and can be used for enteric coating and delayed release of drugs. Rosin and rosin-based polymers have drug delivery applications achieving sustained/controlled release profiles^{6, 7}. One of the good inherent properties exhibited by rosin biomaterials is their film forming ability, utilise in the development of film based drug delivery systems and dosage forms, therefore rosins can be used in the development of transdermal drug delivery systems. Rosin and its derivatives have been used in the formulation of different pharmaceutical preparations⁸. Rosin a natural biomass, is used as a matrix forming polymer for tablet formulations⁹. Rosin has been pharmaceutically evaluated for its encapsulating properties¹⁰. Different investigations have been done to prepare microspheres using rosin as microencapsulating polymer. Rosin-glycerol esters have been reported as micro-encapsulating materials for controlled drug delivery¹¹. Drug release rate are physicochemical properties of drugs, which depend on degradation rate of polymers, and the morphology and size of microparticles. A variety of drugs, regardless of their molecular weights and water solubility, can be loaded into the rosin based microparticles using different manufacturing techniques^{12,13,14,15,16}. In different research, rosin has been evaluated for its binding properties as an anhydrous binding agent^{17, 18}. The biodegradable property of rosin makes it possible to implant them into the body without the need of subsequent removal by the surgical operation. Drug formulated with these polymers can be released in a controlled manner, by which the drug concentration in the target site is maintained within the therapeutic range. The release rates of the drugs from biodegradable polymers can be controlled by a number of factors, such as biodegradation kinetics of the polymers^{19,20,21} physicochemical properties of the polymers and drugs^{22,23}

thermodynamic compatibility between the polymers and drugs²⁴, and the shape of the devices. Thus it can be concluded that rosin and rosin-based polymers have drug delivery applications achieving sustained/controlled release profiles.

Specific properties of rosin: Besides the polymer activity it also act as a active ingredients, such as derivatives of dehydroabietic acid the major component of disproportionated rosin have been reported as anti-tumour compounds²⁵. Studies have been shown that rosin films shown inflammatory reactions similar to PLGA²⁶. Rosin has good emulsifying properties²⁷ and rosin based creams show good spreadability and homogeneity²⁸. Rosin has good quality to enhance skin permeability so the future of transdermal drug delivery looks brighter²⁹. Polymer form of rosin derivative shows the nonlinear thermal stability³⁰.

Application of rosin in pharmaceutical and medical fields: Rosin has been used to prepared spherical microcapsules by a method based on phase separation by solvent evaporation³¹. Rosin based polymer has been used as film coating materials; coated pellets were prepared using diclofenac sodium as a model drug and sustained release of the drug was achieved³². Rosin polymer has used as the transdermal drug delivery system. Rosin combination with polyvinyl pyrrolidone and dibutyl phthalate (30 % w/w) produces smooth film with improved elongation and tensile strength. It have been reported in many studies, that rosin can be used in the design of matrix type transdermal drug delivery system to prolong the drug release. Transdermal patches containing rosin polymer: polyvinyl pyrrolidone (7:3) has prominent pharmacokinetic and pharmacodynamic performance, when evaluated using suitable animal model³³. Rosin has appropriate hydrophobic properties that can be utilized as matrix forming agent of water soluble drug such as diltiazem hydrochloride to prolong the release. The drug release followed first order kinetics and the Higuchi model, thus indicate that there was no erosion of the matrix and the tablet maintained its shape and surface area³⁵. Rosin has been used to prepare aceclofenac sustained release microspheres (as encapsulating polymer). Study easily predict the fact that drug: polymer ratio significantly affect the drug entrapment efficiency of prepared microspheres. The release rate of drug from the microspheres can be controlled for about 24h. It can be concluded that appropriate variation in the stabilizer and proportions of drug: polymer can lead to a product with desired controlled release features³⁵. Derivatives of rosin polymer (RD-1 and RD-2) had been synthesized in the laboratory and evaluated for physicochemical properties, polydispersity (M_w/M_n), molecular weight (M_w), and glass transition temperature (T_g). The derivatives of rosin were further evaluated for pharmaceutical film coating by characterizing the release of a model drug (diclofenac sodium) from pellets coated with the derivatives. It has been found that Pellet film coating could be achieved without agglomeration of the pellets within a reasonable operation time and drug release was sustained up to 10 h with the two rosin derivatives. These results suggest the application of rosin derivatives (RD-1 and RD-2) for film coating³⁶. Rosin is detected in all diapers, in these more rosin was found on top layer and close contact with the

skin. Despite of these have minimal risk of induction of sensitization to rosin allergens in diapers. These materials are not only used for infant diapers but also for feminine hygiene product³⁷. Hydrogenated rosin has prominent film-forming properties and utilised as moisture-protective hydrophobic film-coating materials³⁸.

CONCLUSION

It can be concluded from the whole discussion that rosin obtained from *Pinus palustris*, has good potential as a pharmaceutical excipients in term of biodegradability, ease of availability, matrix forming agent, coating agent, microencapsulating agent and binding agent. It had been found anti-inflammatory and antitumor activity. Its semisolid preparation such as skin cream shows good homogeneity and spreadability. It has prominent property for the sustained release drug system with most of the drug and dosage form. Beside these activities it has many traditional uses.

Acknowledgement: Authors are highly thankful to Department Of Pharmaceutical Technology, Meerut Institute of Engineering and Technology for providing necessary guidance and facilities at the time of work.

REFERENCES

1. Baveja SR, Ranga RKV, Arora J, Examination of natural gums and mucilages as sustaining materials in tablet dosage forms, J Pharm Sci, 51(4), 1989, 115-118.
2. Kakkar AP, Singh M, Medirrata A, Formulation optimization of diltiazem Hydrochloride matrix tablets containing modified isphagula husk using factorial design, Dev Ind Pharm, 23(11), 1997, 1055-1061.
3. Jain RA, The manufacturing techniques of various drug loaded biodegradable poly (lactide-coglycolide) (PLGA) devices, Biomaterials, 21, 2000, 2475-2490.
4. Berkland C, King M, Cox A, Kim K, Pack DW, Precise control of PLG microsphere size provides enhanced control of drug release rate, J. Control. Release, 82, 2002, 137-147.
5. Fulzele SV, Satturwar PM, Dorle AK, Studies on in vivo biocompatibility of novel biomaterials, Eur J Pharm Sci, 20, 2003, 53Y61.
6. Pathak YV, Shinghatgiri M, Dorle AK, In vivo performance of pentastergum coated aspirin microcapsules, J Microencapsul, 4, 1987, 107Y110.
7. Sheorey DS, Dorle AK, Release kinetics & drugs from rosin-glycerol ester microcapsules prepared by solvent evaporation technique, J Microencapsul, 8, 1991, 243Y246.
8. Shirwaikar AA, Reddy N, Rosin, a polymer for micro encapsulation of Diltiazem Hydrochloride for sustained release by emulsion solvent evaporation technique, Ind J Pharm Sci, 62(4), 2000, 308-310
9. Prabu SL, Shirwaikar AA, , Shirwaikar A, Ravikumar G, Kumar A, Jacob A, Farmulation and evaluation of

- oral sustained release of Dildiazem Hydrochloride using rosin as matrix forming material, *ARS Pharmaceutica*, 50, 2009, 32-42.
10. Sheorey DS, Dorle AK, Effect of solvents on the characteristics of rosin walled microcapsules prepared by a solvent evaporation technique, *J Microencapsul*, 8(1), 1991, 71-78.
 11. Sheorey DS, Dorle AK, Rosin coacervate microcapsules: effect of solvent on phase separation of rosin, *J Microencapsul*, 10(2), 1993, 209-214.
 12. Felder CB, Blanco-Prieto M J, Heizmann J, Merkle H P, Gander B, Ultrasonic atomization and subsequent polymer desolvation for peptide and protein microencapsulation into biodegradable polyesters, *J. Microencapsulation*, 20, 2003, 553-567.
 13. Kiyoyama S, Shiomori K, Kawano Y, Hatate Y, Preparation of microcapsules and control of their morphology, *J. Microencapsulation*, 20, 2003, 497-508.
 14. Sinha VR, Trehan A, Biodegradable microspheres for protein delivery, *J. Control.Release*, 90, 2003, 261-280.
 15. Sinha VR, Goyal V, Bhinge JR, Mittal BR, Trehan A, Diagnostic microspheres: an
 16. Overview, *Crit Rev Ther Drug Carrier Syst*, 20, 2003, 431-460.
 17. Wang J, Chua KM, Wang CH, Stabilization and encapsulation of human immunoglobulin G biodegradable microspheres, *J. Colloid Interface Sci*, 271, 2004, 92-101.
 18. Pathak YV, Dorle AK, Rosin and rosin derivatives as hydrophobic matrix materials for controlled release of drugs, *Drug Dev Ind Pharm*, 6(3), 1990, 223-227.
 19. Ramani CC, Puranik PK, Dorle AK, Study of maleoabietic acid as matrix forming material, *Int J Pharm*, 1, 1996, 344-352.
 20. Cicek H, Tuncel A, Tuncel M, Piskin E, Degradation and drug release characteristics of
 21. monosize polyethylcyanoacrylate microspheres, *J. Biomater. Sci. Polym. Ed*, 6, 1995, 845-856.
 22. Mi FL, Lin YM, Wu YB, Shyu SS, Tsai YH, Chitin/PLGA blend microspheres as a biodegradable drug-delivery system: phase-separation, degradation and release behaviour, *Biomaterials*, 23, 2002, 3257-3267.
 23. Zhang Y, Chu CC, In vitro release behavior of insulin from biodegradable hybrid hydrogel networks of polysaccharide and synthetic biodegradable polyester, *J. Biomater. Appl*, 16, 2002, 305-325.
 24. Abraham GA, Gallardo A, San Roman J, Fernandez-Mayoralas A, Zurita M, Vaquero J, Polymeric matrices based on graft copolymers of PCL onto acrylic backbones for releasing antitumoral drugs, *J. Biomed. Mater. Res*, 64A, 2003, 638-647.
 25. Calandrelli L, De Rosa G, Errico ME, La Rotonda MI, Laurienzo P, Malinconico M, Oliva A, Quaglia F, Novel graft PLLA-based copolymers: potential of their application to particle technology, *J Biomed Mater Res*, 62, 2002, 244-253.
 26. Liu J, Xiao Y, Allen C, Polymer-drug compatibility: a guide to the development of delivery systems for the anticancer agent, ellipticine, *J. Pharm. Sci*, 93, 2004, 132-143.
 27. Kinouchi Y, Ohtsu H, Tokuda H, Nishino H, Matsunaga S, Tanaka R, Potential antitumor-promoting diterpenoids from the stem bark *Picea plehni*, *J. Nat. Prod*, 63(6), 2000, 817-820.
 28. Nakagaveat L, U.S.Patent, 5, 478,567D, December 6, 1995.
 29. Mandaogade PM, Satturwar PM, Fulzele SV, Gogte BB, Dorle AK, Rosin derivatives: novel film forming materials for controlled drug delivery, *React Funct Polym*, 50(3), 2002, 233-242.
 30. 28. Park JH, Ye M, Park K, Biodegradable Polymers for Microencapsulation of Drugs, *Molecules*, 10(1), 2005, 146-161.
 31. Bohme K, Buprenorphine in a transdermal therapeutic system--a new option, *Clin Rheumatol*, 21, 2002, Suppl 1: S13-16.
 32. Pathak YV, Dorle AK, Rosin and rosin derivatives as hydrophobic matrix materials for controlled release of drugs, *Drug Des Delivery*, 6, 1990, 223-227.
 33. Sheorey DS, Dorle AK, Preparation and in vitro evaluation of rosin microcapsules: solvent evaporation technique, *J Microencapsul*, 7(2), 1990, 261-264.
 34. Satturwar PM, Mandaogade PM, Fulzele SV, Darwhekar GN, Joshi SB, Dorle AK, Synthesis and evaluation of rosin-based polymers as film coating materials, *Drug Dev Ind Pharm*, 28(2), 2002, 381-387.
 35. Prashant MS, Suniket VF, Avinash KD, Evaluation of polymerized rosin for the formulation and development of transdermal drug delivery system: A Technical Note, *AAPS PharmSciTech*, 6(4), 2005, E649-E654.
 36. Kim H, Fassih R, New ternary polymeric matrix system for control drug delivery of highly soluble drugs, *Pharm Res*, 14, 1997, 1415-1421.
 37. Lakshmana PS, Shirwaikar AA, Shirwaikar A, Kumar A, Formulation and evaluation of sustained release microspheres of rosin containing aceclofenac, 50(2), 2009, 51-62.
 38. Fulzele SV, Satturwar PM, Dorle AK, Polymerized rosin: novel film forming polymer for drug delivery, *Int. J. Pharm*, 249(1-2), 2002, 175-184.
