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Review Article

ROLE OF ROSIN IN CONTROLLED AND TARGETED DRUG DELIVERY

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ABSTRACT

The employment of natural polymers in sustained and controlled drug delivery systems continues to be a field of research. Rosin is on such polymer which is a clear or semi-transparent thermoplastic solid. It occurs naturally in oleoresins of pine tree (*Pinus soxburghi* and *Pinus toeda*, family Pinaceae). 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. Reader can get surely the glimpses of its pharmaceutical versatility. This article focuses a general idea regarding rosin and its polymer derivatives.

Key words: Rosin, Gum rosin, Controlled drug delivery, *Pinus palustris*, Biodegradable, Natural polymer

INTRODUCTION

Polymers are long chain like molecules with repetitive structural units. Since last two decades application of polymers in Pharma field has increased immensely so as to achieve controlled release characteristics. The term *terpene* refers to one of the largest families of naturally occurring compounds bearing enormous structural diversity, which are secondary metabolites synthesized mainly by plants, but also by a limited number of insects, marine microorganisms and fungi.[1] Rosin also known by the name of colophony, is the designation traditionally given to the nonvolatile residue obtained after the distillation of volatiles from the resin exuded by many conifer trees, mostly pine.

Natural polymer Rosin

Rosin (also known as colophony) is a solid resinous material obtained from the oleoresin (tree sap) of live pine trees (called gum rosin), the stump wood of dead pine trees by solvent extraction (called wood rosin), and in the pulp paper recovery process (called tall oil rosin). The rosin is used directly in the manufacturing of adhesives, inks, rubber compounds, paints & coatings, etc., or modified as resins to give more specific characteristics to the rosin to improve or change their stability, aging, color, tackiness. Rosin is a solid resinous mass obtained naturally from pine trees. Principally it contains resin acids (abietic and pimaric) and Rosin is a low molecular weight (MW = 400) polymer exhibiting excellent film-forming

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property. It is primarily composed of abietic and pimaric acid, which contain 2 reactive centers: the carboxylic group and the double bonds.[2] Rosin (including gum rosin, Wood rosin and tall rosin) is an exudate from pine trees and other plants. The major components of rosin are resin acids: primarily abietic acid (AA) and levopimaric acid. The presence of a carboxyl group and/ or conjugated double bonds in their structures imparts them tunable chemical reactivity: e.g. derivation of a vinyl group. Rosin and its derivatives, produced millions of tons annually, are generally used as ingredients for inks, vanishes, adhesives, paper size, cosmetics, medicines, chewing gums, etc. Some of them are used as additives or modifying agents for the improvement of the properties of synthetic polymers. However, the use of rosin as renewable resources for the preparation of Well-defined synthetic polymers (e. g. homopolymers and block copolymers) has not yet been explored. The major reason behind this is that most rosin based polymers are prepared by step growth polymerization or free radical polymerization that lack controls on the polymer structures at molecular level, molecular Weight, molecular Weight distribution and functionality. The absence of the tunability of these parameters limits these polymers used for broader and promising alternatives to petroleum based polymers such as thermoplastic resins, thermoplastic elastomers, polymeric varnishes, polymeric Wax, adhesives, coatings, printing inks to shape memory polymers, polymer nanocomposites, pharmaceutics, anti-fouling materials, etc.[3] Six polymers include levopimaric acid, abietic acid, dehydroabietic acid, hydroabietic acid, pimaric acid, isopimaric acid, and mixtures thereof due to their availability commercially at various purities.

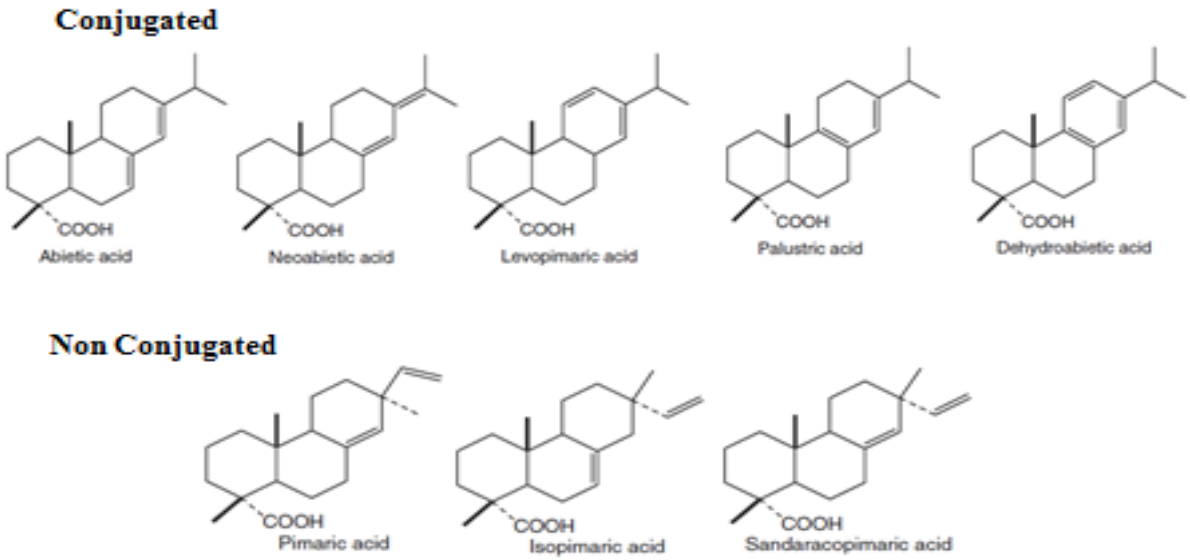

Figure 1: Structure of conjugated and non-conjugated rosin acid derivatives[1]

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The chemical modifications[1, 2, 4] of these molecules which have been thoroughly studied include:

- ✓ The oxidation of one unsaturation to give an endoperoxide;
- ✓ The aromatization of the rings through dehydrogenation and the subsequent functionalization of the ensuing aromatic moieties;
- ✓ The hydrogenation of one or both unsaturations;
- ✓ The isomerization relative to the position of the unsaturations;
- ✓ The Diels – Alder (DA) reaction with dienophiles;
- ✓ The reactions with formaldehyde and phenol;
- ✓ The preparation of salts of the carboxylic acid.

Properties of Rosin [1, 4-9]

1. Rosin is brittle and friable, with a faint piney odor.
2. It is typically a glassy solid, though some rosin will form crystals, especially when brought into solution.
3. The practical melting point varies with different specimens, some being semi-fluid at the temperature of boiling water, others melting at 100°C to 120°C.
4. It is very flammable, burning with a smoky flame, so care should be taken when melting it.
5. It is soluble in alcohol, ether, benzene and chloroform.

Pharmacological utility of rosin

Rosin has been used in endodontic retreatment (repeated root canal procedure) to soften or dissolve the rubbery latex (gutta-percha) in the root canal cavity. Rosin is mainly used as a counter-irritant and rubefacient in treating rheumatism and aching muscles.[10] In Chinese medicine, gum turpentine and rosin (mainly from *Pinus Tabulaeformis* Carr., *P. Massoniana* Lamb., and *P. Yunnanensis* Franch) have been used for centuries in treating rheumatism, stiff joints, toothache, boils, and sores.[11, 12] Furthermore rosin is used in treating ringworms, chronic bronchitis, and neurogenic dermatitis, among others. They are used both internally and externally.[13] Besides the polymer activity it also act as an active ingredients, such as derivatives of dehydroabietic acid the major component of disproportionate rosin have been reported as anti-tumour compounds.[14]

Pharmaceutical applications of rosin

Rosin is used as an ingredient in many ointments, liniments, and lotions for treating minor aches and pains as well as colds. Rosin is an ingredient in some soaps and ointments; it is also used as a fixative in perfumes.[10, 13] Many recent studies have focused on the use of rosin-based polymers for drug delivery in the form of enteric coating, cream bases, and nanoparticles.

1. Microencapsulation

Potential of rosin and its derivatives were ascertained to check its microencapsulation ability.[15] Sustained release diclofenac sodium microcapsules were prepared using polymerized rosin as a novel wall-forming material by a solvent evaporation technique.[16] The prepared microcapsules were evaluated for size, shape, drug content and in vitro drug release. The morphology of microcapsules was characterized by scanning electron microscopy. The microcapsules show sustained release

ISSN 2319-1082

curves at pH 7.4 phosphate buffer for up to 10 h which follows the Higuchi-order release pattern.[17]

2. Matrixing agent

Sustained release matrix tablets were developed using gum rosin and its combination with different polymers by direct compression methods.[18] The drug release of optimized formulation follows the Higuchi kinetic model, and the mechanism is found to be non-Fickian/anomalous according to Korsmeyer–Peppas equation. Compared to conventional tablets, release of losartan potassium from these matrix tablets was prolonged, leading to achieve an effective therapy with low dosage of the drug, to reduce the frequency of medication. Sustained release matrix tablet of Pramipexole Dihydrochloride was prepared using rosin. The drug release followed zero order and found to be diffusion controlled with erosion having high correlation for Higuchi related pattern.[19]

3. Film forming material

Rosin and its derivatives were investigated for enteric coating.[20] Fulzele et al. (2002) have investigated film forming and coating properties of Glycerol ester of maleic rosin (GMR) and Pentaerythritol ester of maleic rosin (PMR).[21] Films were produced by solvent evaporation technique on a mercury substrate using Dibutyl sebacate as plasticizer as it increase film elongation and decrease the Young's modulus, making the films more flexible and thereby reducing the brittleness.[17] Diclofenac sodium-layered pellets coated with GMR and PMR film formulations showed sustained drug release for up to 10 hours.[22, 23] Two PEGylated derivatives of rosin (PD) were investigated for its sustain release film forming ability. Dissolution of diclofenac sodium (DS) and propranolol hydrochloride (PHL) as model drugs was studied from coated pellets. The dissolution data followed zero order, Baker-Lonsdale equation and Hixon-Crowell equation of release kinetics with high correlation coefficients. The mechanism of drug release from these coated systems however followed class II transport ($n > 1.0$). The derivatives investigated could successfully retard release of the model drugs and offers an alternative to the conventionally used polymers.[24] Damar Batu was utilized as film former in pellete coating. The core of pellet was prepared using Diclofenac sodium (10% w/w) as a model drug by extrusion and speronization. The drug containing pellets were coated using DB plasticized film-coating solutions. DB seems to be a promising film former for pharmaceutical coating due to its reasonably good mechanical properties, low water vapor transmission and sustained release capability.[25]

4. Transdermal drug delivery

Polymerized rosin (PR) was investigated for its use in transdermal drug delivery systems. Diltiazem hydrochloride PR patches were prepared with polyvinyl pyrrolidone (PVP). The release rate of drug from films and permeation across skin increases with increase in drug and PVP loading but is independent of film thickness. Patches containing PR:PVP (7:3) show promise for pharmacokinetic and pharmacodynamic performance evaluation in a suitable animal model.[26]

5. Semisolid preparation

ISSN 2319-1082

Various rosin polymers based on glycerol, sorbitol and pentaerythritol were prepared and screened for efficacy. Among these polymers, polymer2 (glycerol-baseids) reported to produce creams with a better stability and release profile as compared to other creams. The creams were formulated employing polymer (P2) and Tween 60 as surfactants. The stability of the prepared creams as well as the diclofenac diethyl ammonium release pattern was investigated using particle size analysis, conductivity, relative dielectric constant, Spreadability and irritation potential measurement and was compared with that of creams containing Tween 60 prepared in the laboratory. The release of the drug, diclofenac diethylammonium was Measured after eight hours and compared with a standard cream and a marketed cream.[27]

6. Taste Masking

Taste Masking Rosin - 134 is derived from crosslinked polymer of acrylic acid and has a K + ionic form. Taste Masking Rosin - 134 forms complex with drug & mask it's bitter taste. This complex formed does not dissociate in saliva pH but, dissociate in acidic pH of stomach. Thus this complex is tasteless without affecting its bio availability. This technique helps to formulate palatable & chewable tablets, dispersible tablet & suspensions of bitter taste drugs.[28] Rosin, and synthetic polymer ethyl cellulose based microspheres of ambroxol hydrochloride were prepared by emulsion solvent evaporation technique.[29] Sensory studies in healthy human volunteers indicated that the taste and palatability were significantly improved by microencapsulation.

Conclusion

Rosin [also known as colophony has achieved much attention since last decades as controlled delivery polymer. All rosins are made up of 90-95% of diterpenic monocarboxylic acids, or resin acids, $C_{19}H_{29}COOH$, in different specific molecular architectures. It has prominent property for the sustained release drug system with most of the drug and dosage form. The cardinal features of rosin for different type of drug delivery has been highlighted in this work.

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