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Polymer Grafting-An Overview

Tibey Mary Koshy¹, D V Gowda*¹, Sweety Tom¹, Godugu Karunakar¹, Atul Srivastava¹
and Afrasim Moin²

1.Dept. of Pharmaceutics, JSS University, JSS College of Pharmacy, SS Nagara, Mysore -
570015, Karnataka, India

2.Department of Pharmaceutics, College of Pharmacy, Hail University, Hail-81442, Saudi
Arabia

ABSTRACT

Polymer grafting open a new window to pharmaceutical formulation. This article review about the different natural polymer and their application in pharmaceutical industry. Techniques such as grafting, crosslinking, blending and composite formation techniques are accustomed to modify the polymer. Recently, polymer grafting method received a wide attention than the other methods employed in the modification of the polymer. Polymer grafting can be achieved by covalent bonding of monomer to the polymer. In this review, techniques such as chemical grafting, radiation grafting etc. are also discussed.

Keywords: Natural, polymer, grafting, techniques, modification.

*Corresponding Author Email: dvgowdajssuni@gmail.com

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INTRODUCTION

Polymers are generally used in the pharmaceutical industries due of their unique properties. A polymer can be defined as a macromolecule which is made up of many repeated subunits¹. The term "polymer refers to a molecule whose structure consists of multiple repetition units, from that originates a characteristic of high relative molecular mass and attendant properties². Natural polymers have wide applications in food and pharmaceutical industry attributable to their easy availableness, biocompatibility, biodegradability and price effectiveness. Properties of the polymer can be improved by the modification of polymer which can be achieved by various techniques like grafting, crosslinking, blending and composite formation. At present, polymer grafting has been obtaining number of application. Grafting is a process where a parent polymer is employed as a backbone onto which branches of second polymer are connected at different points. In other words, polymer grafting is a method in which monomers are covalently bonded onto the polymer chain Polymer grafting improves the functional properties of the polymer such as sulfonation, phosphorylation, carboxymethylation and acetylation have been done⁶. Among these methods, carboxymethylation is commonly used due to its ease of processing, lower cost and versatility. Aqueous solubility and gelling behavior of polysaccharides can be improved by carboxymethylation³. Studies also proved that carboxymethylation of polymer helps to modify the drug release rate⁴. Kanika Thakur et.al, says carboxymethylation of amylopectin can be used for preparing polyelectrolyte nano particulate drug delivery system⁵. Polymer grafting enhances their biological properties and pharmacological applications⁶. Modification of polymer enhances antiproliferation of cancer cells, antioxidant activities and also decreases the viscosity⁶. In this review, we discuss about the different grafted natural polymer and their uses, grafting techniques and the application of grafted polymer.

Natural polymer

Many natural gums are modified to improve their properties. Many studies have been carried to study the properties of modified polymers. Guar gum is a natural polymer extracted from seeds of *Cyamopsistetra gonalobus* plant. It consists of a linear backbone of β -1, 4-linked D-mannose units that is arbitrarily connected with α -1, 6-linked galactose units as a side chain⁷. Chemical modification of guar gum improves their application in pharmaceutical industry. Psyllium is natural polymer containing arabinoxylan. Psyllium can be used for the treatment of constipation, diarrhea, irritable bowel syndrome, colon cancer etc. Modification on polymer open a way for the preparation of polyelectrolyte complexes with cationic polymers⁸. Konjacglucomannan (KGM) is

obtained from the tubers of *Amorphophallus konjac* which is a linear random copolymer of β -(1 \rightarrow 4) linked D-glucose and D-mannose⁹. Kobayashi. S et.al concluded in their studies that carboxymethylation of KGM suppresses the intermolecular hydrogen bond interaction and improves the rheological behavior. Xanthan gum has been widely used in cosmetic and pharmaceutical industry. It is employed as suspending, stabilizing, thickening and emulsifying agent by introducing carboxymethyl group into xanthan gum, its drug release pattern has been modified⁴. *Tremella fuciformis* (TP) is an edible mushroom which has many properties such as antitumor, humoral immune responses, hypoglycemic and hypolipidemic activities also find applications in cosmeceutics such as anti-aging and antioxidation effect. Carboxymethylation of TP enhances the potential biological properties¹¹. Carboxymethyl starch (CMS) is a modified starch obtained from potato starch, which is used as an excipient in the pharmaceutical industries¹¹. Agar is a best known gel forming polysaccharide obtained from *Gelidiaceae* and *Gracilariaceae* species, where agarose and agaropectin are the components of agar. After carboxymethylation of agar, the studies showed that there was an improvement in the hygroscopic nature of the gum¹². Fenugreek gum is obtained from *Trigonella foenum-graecum*, has significance for its emulsion stabilizing and water holding capacity¹³. Bassi. P & Kaur.G found that carboxymethylated fenugreek gum possess film forming property and bioadhesive potential. Gellan gum is an anionic exopolysaccharide obtained from the secretion of the microorganism *Pseudomonas elodea*, used as *in situ* gelling agent in ophthalmic formulations and as a sustained release matrix in bead formulation. It was observed that carboxymethyl gellan gum beads releases drug at a quicker rate than gellan gum³.

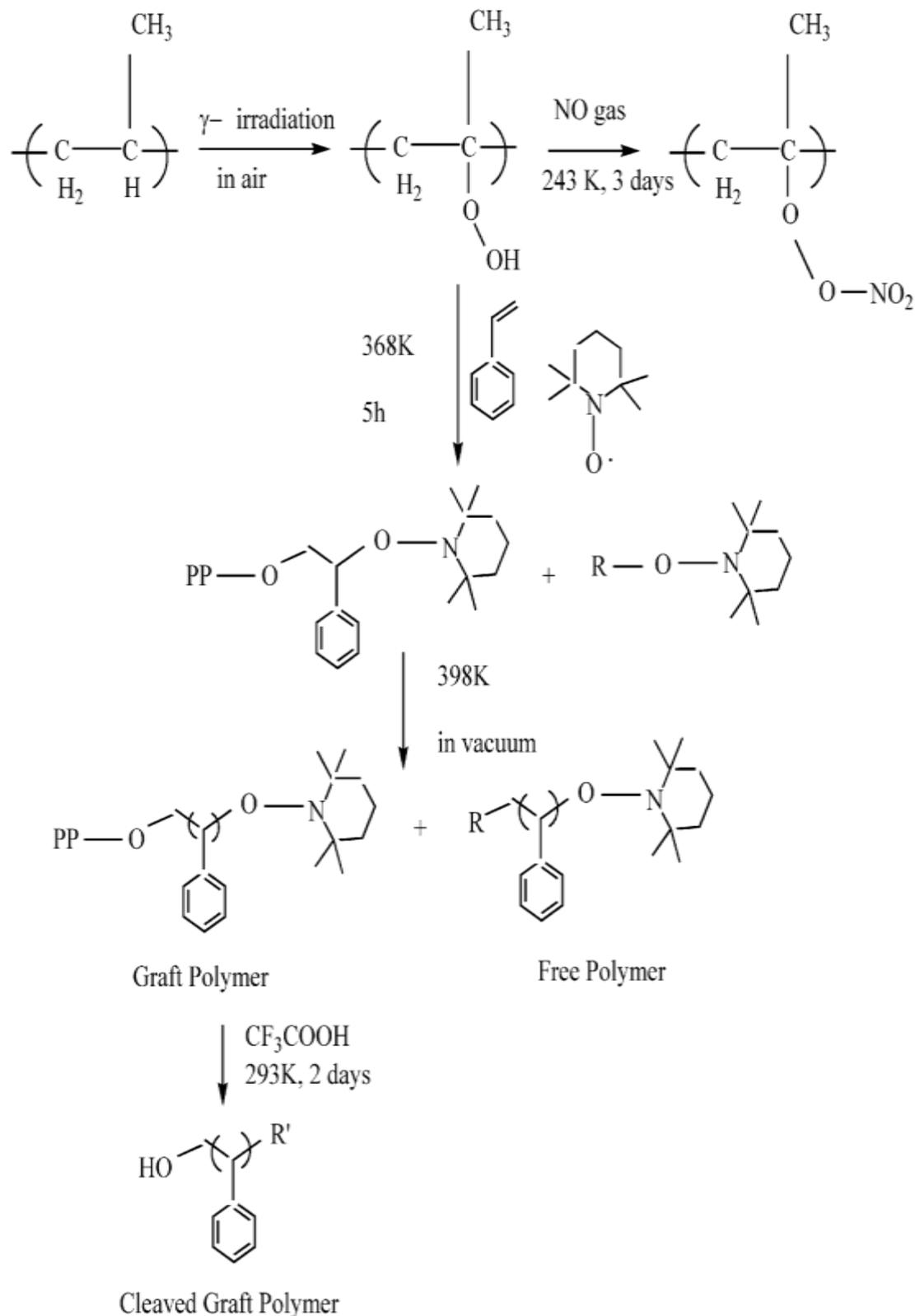


Figure 1: Reaction scheme of graft polymerization of styrene to PP.

Scheme 1. Reaction scheme of graft polymerization of styrene to PP. Reproduced from Macromolecules 2001; 34:2089.

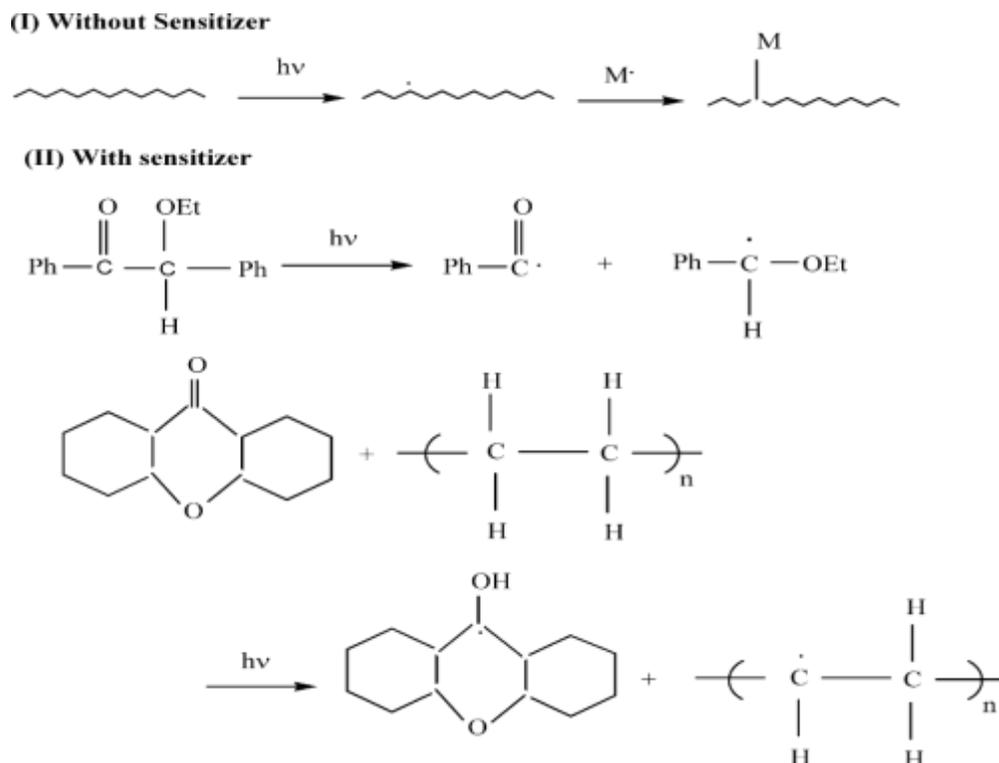


Figure 2: Mechanism for photochemical grafting method.

Scheme 2. Mechanism for photochemical grafting method. (51). Reproduced from Prog Polym Sci 1983; 10:171.

TECHNIQUES OF GRAFTING

Polymers can be grafted by different techniques such as chemical, radiation, photochemical, plasma-induced and enzymatic grafting¹⁶.

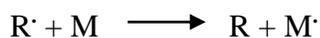
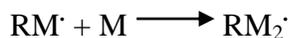
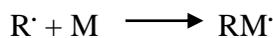
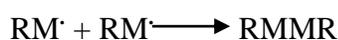
Chemical grafting

Chemical grafting is widely used method of grafting which can be established through free radical generation, ionic generation method and through living polymerization. In chemical method, grafting by free radical technique is initiated by an initiator, which react with the polymer to form grafted polymer whereas in ionic generation method, grafting occur through an ionic mode. Grafting can also be carried out by atom transfer radical polymerization¹⁶.

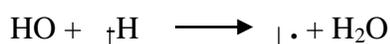
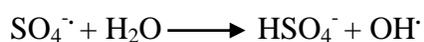
Free radical generation method

Initiator chemicals are used to initiate free radicals in chemical grafting process. The reaction involves transfer of high energy radical to substrate polymer, which reacts with monomers to cause modification to the polymer. Radicals are formed by two methods:-direct and indirect methods.

In direct methods, radicals are formed on the initiator chemical. In this process, free radicals formed through three steps, namely, initiation, propagation and termination processes. I_2 is the initiator chemical, R is the free radical and M is the monomer¹⁷.

A) Initiation step:**B) Propagation step:****C) Termination step:**

In indirect method, radicals are formed through redox reaction. An example for indirect method is the production of $SO_4^{\cdot-}$. Persulphate and a ferrous ion act as a source of $SO_4^{\cdot-}$.¹⁸



(-H is the polymer and M is the monomer)

The propagation and termination steps are similar to the previous method.

Free radical grafting method have several limitations such as:

- Initiator is required to initiate the process
- Termination step can lead to unreactive polymer.
- Grafted product is of broad molecular distribution
- Time invariant degree of chemical change.

Living Polymerization grafting method

Transfer and termination reactions of the process are controlled than the conventional radical grafting method. In living polymerization, results in living polymers with regulated molecular weights and low polydispersities¹⁹⁻²². Controlled free radical polymerization may be effectively achieved through atom transfer radical polymerization (ATRP). It proceeds until all monomers have been consumed and further addition leads to polymerization^{26, 27}.

Sakaguchi and Shimada reported the grafting of polystyrene on a polypropylene backbone can be carried out with 2,2,6,6-tetramethyl-1-piperidinoxyl (TEMPO), by using γ -irradiation in air was

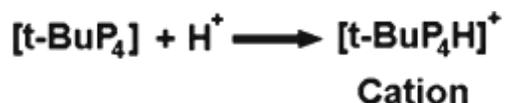
used to form a PP macromolecular initiators, after which TEMPO was used to control the grafting polymerization (scheme 1)²⁸.

The ATRP/controlled living radical polymerization technique would provide a means of expanding the versatility of macromonomer method, because it increases the number of monomers available for making macromonomers.

Limitation of this method is selection of suitable ligands is critical and the reaction has to take place in the absence of oxygen or some reducing agents.

Ionic grafting

Chemical grafting of the polymer can be achieved through ionic mode. Ionic grafting is similar to free radical generation method but in this method chemical initiator do not form free radicals, instead they form cationic or anionic centers which will initiate the grafting process. Tertiary butyl phosphazene (t-BuP4) have been used in the anionic modification of polyethylene oxide by reacting with an acid, generates a cationic center on the initiator molecule²⁹.



RADIATION GRAFTING

Free radical grafting

The irradiation of macromolecules results in homolytic fission and thus free radicals are formed on the polymer. An initiator chemical is not required in radiation grafting. Radiation grafting is a simple, accurate and easy to control process. This process doesn't require catalyst or initiator to initiate the process. Free radicals are generated due to absorption of energy by the polymer.³⁰⁻³³. This grafting process occur in three steps: (a) pre-irradiation (b) peroxidation and (c) simultaneous radiation or mutual irradiation technique.

Pre-irradiation technique:

The polymeric backbone is irradiated with vacuum or inert gas to generate stable free radicals. Then the irradiated polymer substrate is treated with monomer at elevated temperature³⁴⁻³⁸.



(| - H is the polymer and M is the monomer)

Advantages:

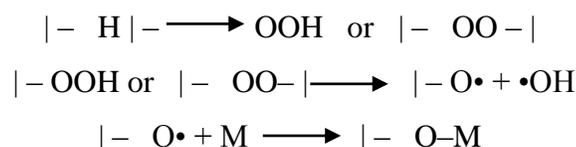
Homopolymer formation doesn't occur since monomer is not exposed to radiation.

Disadvantages:

If the polymer is a degrading type, then direct irradiation results in scission of the base polymer which brings about the formation of block rather than graft copolymers.

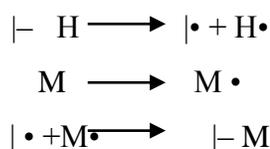
Grafting reaction will not follow if the substrate polymer does not have the ability to trap the radicals for a long enough time.

Peroxidation technique: In the presence of air or oxygen, the trunk polymer is subjected to high - energy radiation which leads to the formation of hydroperoxides or diperoxides which depends on the nature of the polymeric backbone and irradiation conditions. Then the stable peroxy products are treated with the monomer at higher temperature. Grafting is initiated when the peroxides undergo decomposition to generate radicals³⁹⁻⁴¹.



Advantages:

- 1) Intermediate peroxy trunk polymers can be stored for long period of time before the final grafting step.
- 1) Mutual irradiation technique: In this technique, the polymer and the monomers (present as vapor, liquid or solutions) are irradiated simultaneously to form free radicals and subsequent addition⁴²⁻⁴⁷.



Ionic grafting

Radiation grafting can also occur through anionic mode. In this process, the ions formed through high-energy irradiation. Cationic or anionic are the two different types of grafting employed. In the first step, polymeric ion is formed due to the irradiation of the polymer, and then the polymeric ion is made to react with the monomer to form the grafted co-polymer⁵².

Advantages:

- High reaction rate

Photochemical grafting

Photochemical grafting can be achieved through sensitizer or in the absence of sensitizer. In this process, grafting occur due to the absorption of light by the chromophore, moves to the excited state, where it get dissociated into reactive free radicals. If the free radicals are not formed through

bond rupture, the process can be initiated by the addition of photosensitizers such as benzoin ethyl ether, dyes etc. Then the free radicals react with monomer to form grafted polymer⁴⁸⁻⁵⁰.

Plasma radiation grafting

Grafting is initiated by the plasma. In this methodology, electrons are accelerated from the plasma have adequate energy to induce cleavage of the chemical bond of the polymer, ends in the formation radicals to initiate the graft co-polymerization. This method can be carried out without adding any photosensitizer. But this method is restricted to surface grafting^{53, 54}.

Enzymatic grafting

In enzymatic grafting process utilizes enzyme to initiate the grafting process. For example, tyrosinase will convert phenol into reactive o-quinone, which undergoes consequent reaction with chitosan⁵⁵.oxidative enzymes such as peroxidases or laccases has been employed in grafting of biopolymer. These enzymes generate radicals on polymer backbones which may then react with monomer to attain the grafting technique.

CONCLUSION

The discussion show that grafting of the polymer open a wide window of application in pharmaceutical industry. In this review article, we have mentioned the importance of grafting of natural polymer. Second part of the article review about the different techniques of polymer grafting. Apart from the grafting techniques, researchers must take some measures to develop biodegradable polymers to minimize the environmental pollution.

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