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A SYSTEMATIC REVIEW ON GRAFTING TECHNIQUES AND THEIR APPLICATIONS WITH REFERENCE TO NATURAL GUMS AND MUCILAGE

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Abstract

Gums and mucilage are used in pharmaceuticals, cosmetics as well as in textile industries due to their vast properties such as gelling agent, binder, thickener, disintegrating agent and many more. But even after having immense useful properties, various limitations are also there like loss of viscosity while storage and prone to microbial contamination. To overcome these problems the gums needs to be modified for better stability, rigidity and compatibility by using different techniques such as grafting, curing, blending, cross linking, which can be done by using acrylamides, methyl methacrylate, monochloroacetic acid. Among all, graft copolymerization is the most convenient and it can be performed by employing microwave methods, enzymatic process and using various chemicals for example ceric ammonium nitrate and potassium persulphate. Modified natural gums can be incorporated in the sustained release drug delivery systems and various formulations such as nanoparticles acrylic acid grafted cashew gum, hydrogel of ranitidine HCl with polyacrylamide grafted karaya gum etc are developed by these techniques. The present review discusses about the importance of gums, various grafting techniques along with details of patents for various polymer-based inventions.

***Keywords* :** Acrylamides, grafting, methyl methacrylate, monochloroacetic acid and nanoparticles

Introduction

Human beings have been gifted with lots of resources in our surroundings to fulfil our needs and maintaining the balance with the nature. As Pharmaceuticals industries are growing, the need of natural polymers (either obtained from gums or mucilage) is increasing for efficient development of novel drug delivery systems (Bhosale *et al*., 2015).

Gums are being obtained by either breaking down the plant's cell wall or making cuts on to the bark of the plant. But mucilage is the product that has been produced by the plant metabolism thus, doesn't require causing any injury to the plants (Malviya *et al*., 2016). The importance of natural polymers over the synthetic polymers are due to their less cost, abundantly available and better biodegradability. But due to having some major limitations like contamination through microbes, alteration in the viscosity during storage leads to need of modification techniques.

Modification methods involve combining of natural polymer with a synthetic polymer using various techniques like grafting, curing, etc. A grafted co-polymer shows macromolecular series with single or multiple types of block molecule series associated to core polymeric backbone chain as various side chains. Graft polymerization is one of the most convenient way to use various natural polysaccharides in extended drug delivery systems. Nowadays in polymer science, the synthesis and use of these grafted copolymers in various applications is major area for the researchers. Employment of peculiar or selected functional groups into the polymer affects the various chemical, physical as well as the rheological properties of the compound (Malviya *et al*., 2016; Adhikary and Kumar, 2015). In comparison with other Asian countries India is a rich source for natural polymers because of the diverse and varying geography and the environment. These are being used in various industries like cosmetics, pharmaceuticals, textiles etc and also have gained interest of many because of their various applications in pharmaceuticals as binders, diluents, thickener in oral liquids, gelling agents in gels, protective colloid in suspensions, base in suppositories and disintegrating agent in tablets (Adhikary and Kumar, 2015; Mishra *et al*., 2008). Diverse applications of these natural polymers have been studied and their advantages are discussed below.

Advantages of natural gums (Goswami and Naik, 2014)

- Natural gums are renewable and biodegradable with minimal or no harmful effects on either human beings or the environment.
- They are non-toxic in nature with better biocompatibility.
- Easily available at low cost.
- As these are procured from edible sources, acceptability by public and patient tolerance is very high.

Limitations of synthetic polymers

- Their synthetic methods involve use of multistep reaction procedures which leads to have harmful effects on chemists as well as their environmental burden
- Are costly
- Causes skin and eye irritation

Problems associated with available synthetic polymers promoted the use of natural polymers with applicable modification. In next section, we will discuss about grafting techniques and its importance.

Grafted copolymer

Grafted copolymer technique consists of the attachment of polymer chains having dissimilar chemical natures at different sites of previously formed polymer backbone. The connected side chains may comprise of a monomeric unit or of a binate mix. The first one (having one monomer) is easier to synthesize and generally happens in a solitary step, nevertheless grafting in the case of binate blend requires to be done in many steps which includes continuous and stepwise addition of the monomers (Adhikary and Kumar, 2015). The diagrammatically representation is shown below in figure 1.

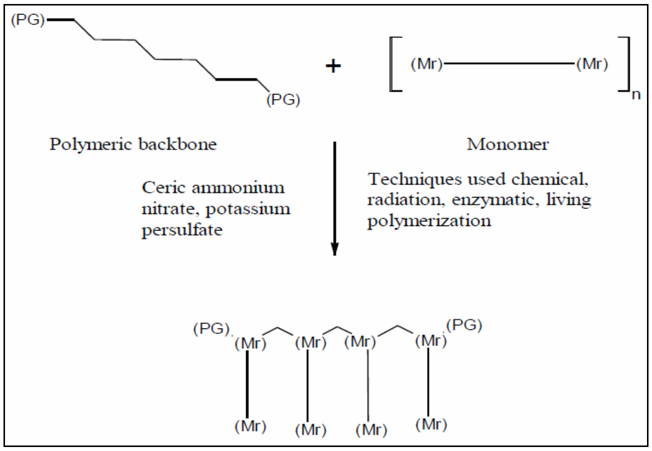

Fig. 1: Diagrammatically representation of process of grafting

Different techniques for grafting

There are numbers of techniques such as microwave methods, enzymatic process and by using various chemicals are available for performing grafting as shown in fig. 2. The detail of each method is discussed separately below.

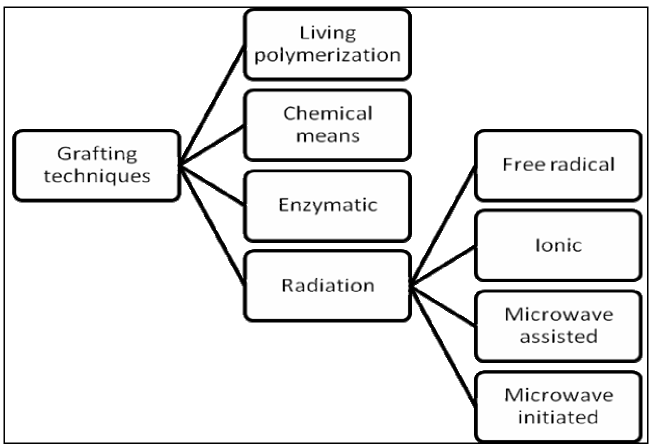

Fig. 2: Illustration of various techniques for grafting (Vijan *et al*., 2012)

1. Grafting through living polymerization: It comprises features of both, the typical free-radical and ionic polymerizations to express free-radical polymerization in a controlled manner. In case of classical free radical polymerization, there is a requirement of constant induction, with annihilation of flourishing chain radicals in pairing or disproportionate reactions, leading to unreactive polymers called dead polymer. In living polymerization, live polymers are produced with synchronized molecular weight and less poly-dispersity (Hong *et al*., 2002).

2. Grafting induced by chemical means: Grafting can be accomplished by chemical means via two main paths such as free radical and ionic. In this process, initiator plays an extremely significant role, as it decides the fate of grafting procedure. Apart from this general free-radical mechanism, atom transfer radical polymerization (ATRP) and grafting in the melt are fascinating techniques for grafting.

3. Grafting by means of enzymes: This process of grafting includes the enzyme that acts as an inducer which begins the chemical grafting on to the preformed polymeric backbone. The modification by enzymes has gained concern of the people, as it requires conditions that are mild and very particular modification of surface, which leads to a non-destructive conversion of the polymeric backbone. This modification technique that is, grafting by enzymes on to the natural products has been studied very well and found several industrial applications. It is a fairly newer technique. In this technique, enzyme begins the chemical or electro-chemical grafting reaction. In a case, tyrosinase which is able to transform phenol into reactive o-quinone, that further went to consecutive non-enzymatic reaction with chitosan (Bhattacharya and Mishra, 2004).

4. Radiation techniques: In this graft copolymerization technique radiations are used which serves as an initiatory system that provides regulated length and numbers of the obtained grafted chains and carried out by carefully choosing the dose and the rate of the dose. Grafting by this technique is the most favourable one. When the electromagnetic radiation crosses the polymeric backbone, it is responsible for production of the active sites that are required for completion of the reaction. This procedure allows maintaining the integrity of the product. Radiation permits to accomplish the reaction at different depths of the already formed polymeric backbone, solely depends over radiation's penetrating power incorporated. Furthermore, in case of the radiation initiated grafting the molecular weight of the developed polymer can also be delimited. And due to these much features, this is one of the most favoured method for graft polymerization (Malviya *et al*., 2016, Mishra and Bajpai, 2006). It is further divided into different subparts which are discussed here.

a) Free radical grafting: Polymers free radicals can be formed by irradiation of the macromolecules due to which homolytic fission occurs. Medium is more important than the use of initiator. There are three ways such as Pre-irradiation, peroxidation followed by mutual irradiation, by which the grafting technique takes place (Curcio *et al*., 2009; Uflyand *et al., 1992*).

b) Grafting by ions: Ions can also be used for the grafting procedure. Various initiators are used for this process that includes organic metallic compounds, sodium naphthalenide and an alkali metal suspension in lewis base.

c) Grafting based upon microwave: In the synthesis of a polymer, microwave radiation can be used as a replacement technique against the conventional procedures used for the graft copolymerization. This microwave stationed synthesis is accepted as it provides better yield, better selectivity, and high rate of reaction. The consumption of energy and solvent is also very less. Due to less waste materials after synthesis of the polymer, it is very much environment friendly. Use of microwave radiations trims the time of reaction and also the communion between the raw material and the harmful organic solvents. This technique does not require severe conditions or elevated temperatures for the modification of biopolymer (Mishra *et al*., 2008).

d) Microwave initiated technique: This technique does not use initiators but use hydroquinones used as radical inhibitor which slow down the grafting process (Kumar *et al., 2012).*

e) Microwave assisted technique: Initiators are used in this technique and by adding up the initiators into the reaction mixture, production of ions takes place that improves the quality of aqueous reaction mixture to transform the microwave energy into heat energy.

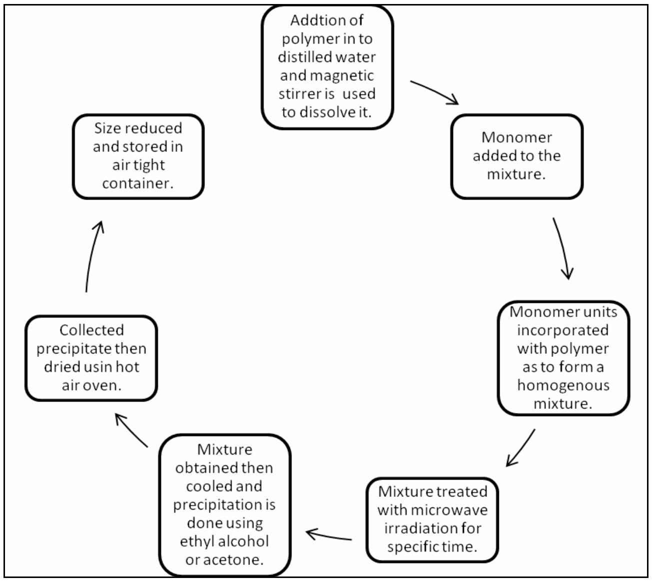

Fig. 3: Microwave based grafting (Malviya *et al.*, 2016)

Various factors affecting the microwave based grafting technique have been illustrated below.

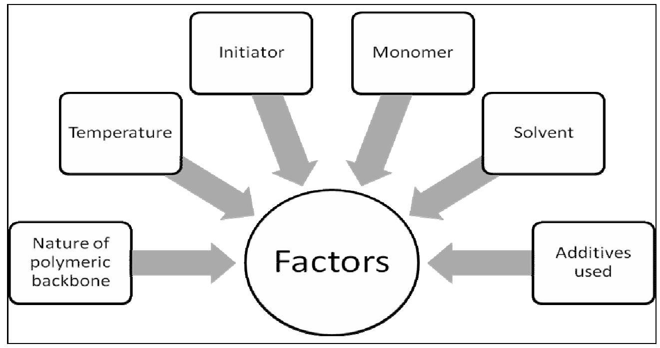

Fig. 4: Factors affecting grafting process (Bhosale *et al.*, 2015)

There are numbers of techniques used for grafting are discussed earlier. Here, we also summarize the details of various naturally available gums and mucilage used for grafting and their uses in various delivery systems are summarized in table 1.

Table 1: Techniques for grafting used and their use in various delivery systems

Gums and Mucilage	Technique for grafting	Uses	References
Xanthan gum	Solution polymerization technique	Sustained drug delivery	Adhikary and Kumar, 2015
Tamarind mucilage	Microwave assisted free radical polymerisation	Sustained drug delivery, rectal drug delivery	Mishra *et al.*, 2008
Gellan gum	Microwave assisted free radical polymerization	Sustained drug delivery	Vijan *et al.*, 2012
Okra gum	Conventional method	Controlled drug delivery	Mishra and Bajpai, 2006
Locust bean gum	Microwave assisted	Sustained drug delivery	Kaity *et al.*, 2013
Guar gum	Chemical modification	Colon delivery, film coating	Sandolo *et al.*, 2007
Cashew gum	Radical polymerization technique	Sustained drug delivery	da. silva *et al.*, 2007

We have also reviewed patents granted for grafted polymers in table 2. These data will help the readers to understand the importance of grafted polymers with their applications.

Table 2: Patents for grafted polymers-based inventions

Patent No.	Publication year	Invention	Reference
US005132284A	1992	Neutrally charged poly amphoteric poly saccharide grafted copolymers.	Tsai, 1992
US005583193A	1996	Polysaccharide grafted polymer and their use in paper making.	Aravindakshaand Singh, 1996
WO2008098019A2	2008	Polymer formulations for bioactive delivery of bioactive agents	Daniloff *et al.*, 2014
US9062130 B2	2015	Cross linking of low molecular weight and high molecular weight polysaccharides preparation of injectable monophase hydrogels, polysaccharides and hydrogels obtained	Leberton, 2010
US9504707 B2	2016	Use of the modified polysaccharides for heparin neutralization	Nawakowska *et al.*, 2016

After discussing various naturally available gums, mucilages and techniques used for grafting, we have also summarized the details of various patents based on their modification techniques.

Table 3: Patents based on modification of techniques

Patent no.	Title	Publication year	Reference
US2644765 A	Modified locust bean gum, solution and process for making LBG solution.	1953	Sweeney, 1953
US3228328	Periodate modified polygalactomannan gum & method for preparation of the same.	1966	Opie and Keen, 1966
US3415927	Heat modified dispersible guar gum.	1968	Samuel *et al.*, 1968
US6398911 B1	Modified polysaccharides containing polysiloxane moieties.	2002	Schroeder *et al.*, 2002

Conclusion

There are many modification techniques including blending, curing other than grafting but modification using grafting techniques show better results due to enhancement of their physical and chemical properties. In comparison between the conventional closed vessel techniques and the microwave based grafting techniques, the microwave-based techniques are better as the polymer gets easily modified. Grafted co-polymers have increased capacity to hold water. These are capable to be accustomed in the controlled and sustained drug delivery systems. Due to the biodegradability, they are non-toxic and compatible to the body fluids. There are various patents that have been granted for the modification techniques as well as for the grafted polymer-based inventions. These grafted polymers are not only found useful in pharmaceuticals but can also be used in various fields.

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