Review Article

Applications of natural polymers in mucoadhesive drug delivery: An overview

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Abstract

Aim of this review is to compile the current literature with special focus on role of natural polymers on mucoadhesive drug delivery system. Mucodhesion refers to bond formed between two biological surfaces or a bond connecting a biological and a synthetic polymer surface. Under this drug delivery, buccal mucosa is the preferred site for both systemic and local drug action because the mucosa has a rich blood supply and it relatively permeable. Different bioadhesive dosages form available in market such as Chewing gum, tablets, Patches, Hydrogel, Thiolated tablets. In this review article the Application of natural mucoadhesive polymers advantages, disadvantages and future prospects in Buccal drug delivery has been discussed.

Keywords*:* Anatomy of oral mucosa, buccal, mucoadhesive polymer, permeation, dissolution.

Introduction

The general availability of drugs taken orally may be limited by the g.i.t transit time of the drug delivery system. This is particularly so far drugs those are majorly absorbed from the intestine. There availability is limited by the residence time of the drugs in or upstream of the small intestine. This type of drug easlity to deliver through mucoadhesive drug delivery systems. In mucoadhesive drug delivery systems basically the drugs are incorporated in a polymer that has the mucoadhesive properties (Chowdary et al., 2000).

Definition of bio adhesion

In bio adhesive drug delivery systems, the term bio adhesion is used to describe the bonding or adhesion between synthetic or natural polymer soft tissues like as epithelial cells. The term mucoadhesion is used to describe adhesion interactions between polymers and mucus or mucosal surfaces (Nagai et al., 1987).

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Advantages

Mucoadhesive dosage forms facilitate increase contact of the formulation with the underlying absorption surface of the body consequently macromolecules such as peptides and proteins are easiliy to absorb in the body. In mucoadhesive formulation developed with penetration enhancers' agents such as sodium glycocholate, sodium tauochaolate, L-Lysophos photidyl choline 9LPLO and protease inhibitors in resulted better absorption of peptides macromolecules into the body. It prolongs the residence time of the dosage form at the site of application, absorption and increase the action of drug (Duchene et al., 1988).

Buccal Drug Delivery and Mucoadhesivity

In buccal drug delivery systems, mucoadhesion property of formulation is the key element. For proper and good mucoadhesion property depends on nature of polymer. The mucoadhesive polymers currently used for the development of different dosages form such as tablets, patches, tapes, films, semisolids and powders. Many studies reported that due to utilization of various mucoadhesive polymers to drug delivery systems, increased the duration of attachment and efficacy of the

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drug. The mucoadhesive polymers should possess some general physiochemical features such as predominantly anionic hydrophilicity with numerous hydrogen bond-forming groups. Natural polymer and its degradation products should be non-toxic, non-irritant and free from leachable impurities.

Natural polymers

The polymers within this category are soluble in water. Matrices developed with these polymers swell when they come in contact an aqueous media with subsequent dissolution of the matrix. The polyelectrolytes widen

Table 1. List of polymers used in formulation of various drug delivery systems.

Name of polymer	Formulation	References
Karya gum	Developed and evaluated gastric retentive gel for rodents in situ, using a mixture of sodium alginate and karaya gum. Feasibility studies were conducted in Sprague-Dawley rats using barium sulfate as a radio-opaque tracer.	Foster et al., 2012 ;Murali Mohan Babu et al., 2002
	Developed modified gum karaya as a carrier for improving the oral bioavailability of a poorly water-soluble drug, nimodipine.	
Xanthan gum	Sustained-release and swelling characteristics of xanthan gum/ethylcellulose-based injection moulded matrix tablets: in vitro and in vivo evaluation.	Quinten et al., 2011 ;Patel et al., 2007 ; Sakeer et al., 2010
	Statistical evaluation of influence of xanthan gum and guar gum blends on dipyridamole release from floating matrix tablets.	
	Xanthan and its binary blends with synthetic polymers to design controlled release formulations of buccoadhesive nystatin tablets.	
Guar gum	Guar gum-based sustained release diltiazem	Altaf et al., 1998; Al-Saidan et al., 2004
	evaluation of guar gum-based three-layer matrix tablets for oral controlled delivery of highly soluble metoprolol tartrate as a model drug	
Tragacanth	Common Natural Ingredients Used in Food, Drugs and Cosmetics	Leung et al., 1980
Pectin	on the gelling behaviour of 'nopal' (Opuntia ficus indica) low metholoxyl pectin	Cárdenas et al., 2008
Chitosan	Propranolol hydrochloride, buccal film	Angela et al., 2011; Furtado et al., 2010; Nafee et al., 2003; Das et al., 2001; Patel et al., 2007; Manasa et al., 2010; Patel et al., 2009; Deshmane et al., 2009; Kumar et al., 2010
	Metoprolol tartarate, buccal patches	
	Cetylpyridinium chloride, buccal patches	
	Curcumin, buccal patches	
	Propranolol hydrochloride, buccal patches	
	Resperidone, buccal patches	
	Salbutamol sulphate, buccal patches	
	Verapamil HCL , buccal patches	
	buccal patches of Lornoxica	
Gum Arabic	Natural gums and modified natural gums as sustained-release carriers	Bhardwaj et al., 2000; Ramakrishnan et al., 2007
	Encapsulation of endoglucanase using a biopolymer gum arabic for its controlled release	
Locust bean gum	Carboxymethyl ethers of locust bean gum	Dey et al., 2011; Bashardoust et al., 2013
	Physicochemical Characterization and Dissolution Study of Ibuprofen Compression-Coated Tablets Using Locust Bean Gum	
Grewia gum	Effect of grewia gum as a suspending agent on ibuprofen pediatric formulation	Ogaji et al., 2011
Bhara Gum	Design and Evaluation of controlled release bhara gum microcapsules of famotidin e for oral use	Nayak et al., 2008
Mango Gum	Evaluation of disintegrating properties of Mangifera indica	Kumar et al., 2011
Gelatin	Sumatriptan succinate, Mucoadhesive bilayered patches	Shidhaye et al., 2008; Khairnar et al., 2009
	Aceclofenac of Mucoadhesive buccal patch	
Fenugreek gum	The Potential of *Trigonella foenumgraecum*	Nayak et al., 2012
	L. Seed Mucilage as Suspending Agent	
Tamarind gum	Various studies have been conducted on the buccal delivery of drugs using mucoadhesive polymers primarily polysaccharides	Bottari et al., 1975

greater mucoadhesive property such as. poloxamer, hydroxypropyl methyl cellulose, methyl cellulose, poly (vinyl alcohol) and poly (vinyl pyrrolidone), have been used for mucoadhesive properties. The natural polysaccharides and its derivatives like chitosan, methyl cellulose, hyaluronic acid, hydroxy propyl methylcellulose, hydroxy propyl cellulose, Xanthan gum, gellan gum, guar gum, and Carrageenan have been utilized in development of ocular drug delivery systems. Cellulose and its derivates have been reported to have surface active property in addition to its film forming capability. Cellulose derivatives with lower surface acting property are normally preferred in ocular delivery systems as they cause reduced eye irritation. Cationic cellulose derivatives (e.g. cationic hydroxyethyl celluloses) have been used in conjunction with various anionic polymers for the development of sustained delivery systems (Shukla et al., 2017; Shukla et al., 2018).

Characteristics of an ideal Mucoadhesive Polymer

An ideal mucoadhesive polymer has the following characteristic

1. They must be nontoxic and should be non-absorbable from the gastrointestinal tract.
2. It must be nonirritant to the mucous membrane.
3. It must preferably form a strong non-covalent bond with the mucin-epithelial cell surfaces.
4. It must adhere quickly to most tissue and should possess some site-specificity.
5. It must allow daily incorporation to the drug and offer no hindrance to its release.
6. The polymer should not decompose on storage or during the shelf life of the dosage form.
7. The cost of polymer should not be very high so that the prepared dosage form remains competitive (Girish et al., 2009).

Disadvantages of Natural polymers (Shirwaikar et al., 2008**)**

1. They are easily to microbial degradation.
2. Batch to batch variation come.
3. The unreserved rate of hydration.
4. Heavy metal adalteration.

Future perception

Natural mucoadhesive polymers increase bioadhesion time of drug molecules; this property of formulation can utilized in wide variety of drugs administration for improvement in specific therapies, efficacy and more general patient compliance. Hence mucoadhesive natural polymers can be used as means of improving drug delivery other than different routes like gastrointestinal, nasal, ocular, buccal, vaginal and rectal. Many prospective mucoadhesive systems are being investigate which may find their way into the market in near future. Natural polymers have vast potential for the delivery of therapeutic macromolecules, genes, and vaccines. Unfortunately, only a few studies have been conducted with new generation mucoadhesive natural polymers for novel drug delivery, and very few papers focus on the changes of structure and rheology of the mucus caused by the mucoadhesive polymer, to what extent the interaction between the polymer and the mucus influences the release of the drugs including in the disease condition. The various sites where mucoadhesive natural polymers have played an important role include buccal cavity, soft palate, gingival, nasal cavity, rectal lumen, vaginal lumen and gastrointestinal tract with recent advancements in the fields of biotechnology and cytoadhesion, the authors believe that there will be both academic and industrial efforts to explore this new area of mucoadhesive like nasal drug delivery, and it might not be too far-fetched to envisage more and more nasal products that employ mucoadhesive polymers.

Conclusion

Mucoadhesive drug delivery system proves to be a only alternative to conventional drugs by popular quality of its

Table 2. Marketed oral mucoadhesive drug delivery systems

Drugs	Dosage form	Type of release	Products name	Manufacturer
Chlorhexidine Hydrocortisone sodium succinate	Oromucosal gel	Controlled	Corsodyl gel	GalaxoSmithKline
Hydrocortisone sodium succinate	Oromucosal pallets	Controlled	Corlan pellets	Celltech
Buprenorphine HCl and Naloxone	Tablet	Quick	Sulbutex	Reckitt Benckiser
Proclorperazine	Tablet	Controlled	Buccastem	Reckitt Benckiser
Testosterone	Tablet	Controlled	Straint SR	Columbia
Zolpidem	Spray	Quick	Zolpimist	Pharmaceuticals NovaDel

ability in overcoming hepatic metabolism, reduction in dose frequencies and enhancing bioavailability. Natural polymers used as mucoadhesive polymers. It facilitates an important tool to improve the bioavailability of the bioactive agent by improving the residence time at the delivery site. Improvement of novel natural mucoadhesive delivery systems are being undertaken so as to understand the various mechanism of mucoadhesion and improved permeation of active agents. Mucoadhesive drug delivery systems required to more work for the development of ideal mucoadhesive polymer which can deliver the drug very easily.

Conflicts of interest: Nil

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