ISSN: 0975-766X
CODEN: IJPTFI
Available through Online
www.ijptonline.com
Review Article

PHARMACEUTICAL SIGNIFICANCE OF NATURAL GUMS: A REVIEW

D.K.Gupta[1]*, Dr.D.K.Agarwal[4], S.Tyagi[1], PrinceP.Sharma[2], R.D.Sharma[1], Dr.Anurag chaudhary[3]
[1]Department of Pharmacy, Faculty of Pharmacy, Bharat Institute of Technology, Meerut, India.
[2]Department of Pharmaceutical science, (FAMS), Gurukul kangri University, Haridwar, India.
[3]Department of Pharmacy, Faculty of Pharmacy, Shubharti University, Meerut, India.
[4]Dr.knmiper, Modinagar, INDIA.
Email: dineshgupta_008@rediffmail.com

Received on 10-05-2013 *Accepted on 22-05-2013*

Abstract

Gums and mucilages are widely used natural materials for conventional and novel drug delivery. To identify the potential of natural polymer in modulation of drug release from the formulation of different dosage form and demonstrate its utility in pharmaceutical drug carrier systems. Polymeric delivery systems are mainly intended to achieve controlled or sustained drug delivery. Physicochemical characterization of the natural gum was done by carrying out solubility test, loss on drying, total ash and acid insoluble ash determination, pH determination, swelling characteristics and micromeritic properties. This article contains the basic information regarding use of different natural polymers in the formulation as a binding agent, suspending agent, disintegrating agent etc. Natural gums could be used for controlled release of both water-soluble and water insoluble drugs. These natural gums have advantages over synthetic ones since they are chemically inert, nontoxic, less expensive, biodegradable and widely available. This article contains the basic concept of natural polymers which is used in sustained-release formulation and also the different types of the same.

Introduction:

Natural gums find wide range of pharmaceutical applications that includes their use as binder, disintegrants in tablets, emulsifiers, suspending agents, gelling agents and also used as sustaining agents in tablets.[1] Synthetic hydrophilic polymers are used more often than natural polymers, but because of cost associated with synthetic polymers, researchers are now showing interest in natural polymers (Non-Synthetic) such as gums. Tamarind[2],*(Tamarindus Indica L.), Bora*

rice, a variety of glutinous rice, Sesame (*Sesamum indicum* L.) etc. Many polymers can be used in the formulation of control release drug delivery system, xanthum and guar gum is the best natural polymer ,which has the wide application in the formulating control release tablets[3].

Natural or modified polysaccharides (guar gum, xanthan gum, locust gum, dextrans, starch, amylose, pectins) degraded by the human colonic flora, have thus been investigated as colonic drug delivery carriers. 0.75 percent polymer containing formulation showed retarded release at the end of 8 hrs. All the batches in first two hours showed very negligible release, then it showed increase in drug release up to 8 hours. Xanthan gum microspheres showed more retarded release than guar gum microspheres. The microspheres are spherical in shape and having rough surface[4]. Locust bean gum is a popular natural polymer which is mostly used in food industry as well as in pharmaceutical industry. This natural polymer is conventionally used as an excipient in manufacturing different formulations which mainly depends on its thickening and gelling property. Locust bean gum can easily be modified to its carboxymethyl derivative which in turn can be used as sustained release delivery carrier as rate controlling polymer. The modified gum shows improved physical properties like good aqueous solubility, acceptable solution viscosity and clarity compared to the native one[5]. The specific application of plant derived polymers in pharmaceutical formulations include their use in the manufacture of solid monolithic matrix systems, implants, films, beads, micro particles, nano particles, inhalable and injectable systems as well as viscous liquid formulations[1-3]. The successful formulation of a stable and effective dosage form therefore depends on the careful selection of excipients. The present trend focuses on an increasing interest in the use of natural ingredients in food, drugs and cosmetics.[5-9] Various properties are there which make locust bean gum a good choice in drug delivery.

• They are biocompatible, biosorbable and biodegradable in nature.

• It is non-teratogenic and non-mutagenic according to Joint FAO/WHO Expert Committee on Food Additives held in Geneva, April'75.

• Acceptable shelf-life.

• Degradation products are excreted readily.

Nowadays a trend has come to modify non-starch polymer in order to modify their physico-chemical properties. Thus the modified natural polymers can be defined as the natural polymers altered to improve their biodegradation profile and

also physico-chemical characteristics. Generally labile polar functionalities are added to the polymer to enhance the degradability of the polymer. The extent and nature of polymer modification is vital as excess modification can hamper the biodegradation and the added functional group may be converted to toxic degradation products[18-21]. This modification of natural polymers is achieved by chemical modification or enzymatic alteration. The chemical modification involves harsh conditions in comparison to the enzymatic method[4].

Natural polymer: Classification[16]

A) Proteins: Collagen, Gelatin

B) Polysaccharides: Agar, Alginate acid, Sodium or Potassium carageenan, Tragacanth, Pectin, Guar Gum, Cassia tora, Xanthan, Gellum Gum

Natural gums used for topical gel:

For the preparation of bioadhesive topical gel natural polymer *aegel marmelos* (plant Bale) was used. Bioadhesive polymers are the agents which increases the contact between the formulation and biological membrane, so as to avoid the fluctuation of formulation and behave as a sustained release formulation. In the present study, prepared bioadhesive topical gel was evaluated with the help of different parameters like drug content, spreadability, extrudability, swelling index study, *in–vitro* drug diffusion study, *in-vitro* drug release kinetic study and *ex–vivo* bioadhesive measurement. On the basis of *in–vitro* drug diffusion study and *ex–vivo* bioadhesive measurement property of gel, we have concluded that natural polymer *aegel marmelos* is the best polymer for the preparation of sustained release bioadhesive topical gel[10]. *In-situ* gelling solutions are one of the most successful means of delivering the drug at ocular site with maximum bioavailability. Pilocarpine *in-situ* gelling solution based on alginate along with novel bioadhesive tamarind gum and widely used bioadhesive, chitosan were formulated. The formulations were tested for drug content uniformity, bioadhesive strength, gelation and *in vitro* release study. Further *in-vivo* miotic test was carried for all formulations[11]. The tamarind gum is good viscosity enhancer and hence it prevents the spillage of the ocular solution out of *cul de sac* thereby preventing loss by drainage and reduction of wash out of topically administered drug[12, 13].

Alginate makes a potential matrix system on undergoing gelation in divalent ions; however addition of other polymers enhances the gel consistency and capacity to sustain drug release.[14]

A similar release pattern was reported for pilocarpine, wherein the initial fast release (burst effect) decreased with an increase in polymer concentration from alginate systems [15].

Natural polysaccharides are complex carbohydrates having good mechanical properties for application as fiber, films, adhesives, rheology modifiers, hydrogels, emulsifiers, and drug delivery agents. Tamarind seed polysaccharide (TSP) is a glucosaminoglycan derivative extracted from the kernel of seeds of *Tamarindus indica* Linn., Family Leguminosae. A polymer consists of cellulose-type spine that carries xylose and galactoxylose substituents. It can be used as a binder in tablets, as a mucoadhesive for buccal or sublingual delivery of drugs, in gastro-intestinal targeting as a bioadhesive tablet, and for ocular delivery of drugs for achieving zero-order controlled release. They also act as a carrier for delivery of certain drugs. TSP future perspective is wide application as a promising polymer in pharmaceutical industry as a novel carrier of drugs in various bioadhesive and other sustained release formulations.[17]

Pectins are anionic polysaccharides extracted from cell wall of most plants. Pectin contains a backbone of α-(1-4)-D-galacturonic acid residues. It readily form gels in aqueous solution in the presence of divalent ions such as free calcium ions, which crosslink the galacturonic acid chains in a manner described by egg-box mode. Pectin undergoes phase transition to gel state in presence of H+ ion when it is administered orally. Calcium ions in the complexed form may be included in the formulation for the induction of pectin gelation. [18]

Xyloglucan is a polysaccharide derived from tamarind seeds and is composed of a (1-4)-β-D-glucan backbone chain, which has (1-6)-α-D xylose branches that are partially substituted by (1-2)-β-D-galactoxylose. Xyloglucan is composed of heptasaccharide, octasaccharide and nonasaccharide oligamers, which differ in the number of galactose side chains. Although xyloglucan itself does not gel, dilute solutions of xyloglucan which has been partially degraded by galactosidase exhibit a thermally reversible sol–gel transition on heating.[19]

Gellan gum (commercially available as Gelrite™ or Kelcogel™) is an anionic deacetylated exocellular polysaccharide secreted by Pseudomonas elodea with a tetrasaccharide repeating unit of one α-L-rhamnose, one β-D-glucuronic acid and two β-D-glucuronic acid residues. Chemical structure of the polysaccharide has a tetrasaccharide repeat unit consisting of two glucose (Glc) residues, one glucuronic acid (GlcA) residue, and one rhamnose (Rha) residue. These are linked together to give a tetrasaccharide repeat unit.[20]

Sodium alginate is a salt of Alginic acid - a linear block copolymer polysaccharide consisting of β-D-mannuronic acid and α-L-glucuronic acid residues joined by 1,4-glycosidic linkages.[21] Aqueous solutions of alginates form firm gels on addition of di- and trivalent metal ions. The results indicated that the alginates form compact structures when the ionic radii of the cation are lower. Changes in the film structure during ionic exchange were studied on the basis of its glass transition temperature (Tg) and heat capacity using differential scanning calorimetry (DSC). Sodium alginate has been employed in the preparation of gels for the delivery of biomolecules such as drugs, peptides and proteins.[22]

The bioavailability of diclofenac sodium in the form of eye drop is very low and when the drug is administered in the form of ophthalmic suspension it lead to irritation due to particle size. So in the present study diclofenac sodium gels were developed with the aim of promoting the prolong release of drug using natural polymer.[45]

Natural gums used for conventional dosage form:

The objective of the present investigation was to develop oral controlled release tablets for nimodipine using a natural gum such as Xanthan gum, Olibanum gum, Locust bean gum. Xanthan gum is a high molecular weight extracellular polysaccharide, produced on commercial scale by the viscous fermentation of gram negative bacterium *Xanthomonas campesteris*. The molecule consist of a backbone identical to that of cellulose ,with side chains attached to alternative glucose residues. It is a hydrophilic polymer, which not only retards the drug release but also provide the time independent release kinetics. [38,39]. Olibanum is a gum resin obtained from *Boswellia serrata,* Roxburgh and other species of Boswellia. The resin contains mainly a resin acid like boswellic acid and a resene olibanoresene in equal proportions. Locust bean gum (LBG) is a plant seed galactomannan, composed of a 1-4 linked ß-D-mannan backbone with 1-6-linked α-D-galactose side group. Longer galactose side chain produce a desirable viscosity which retard the release of drug through matrices[41].Nimodipine (NM) is isopropyl-2methoxyethyl-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5 –pyridine dicarboxylate, a dihydropyridine calcium antagonist. It has a short half-life of 1-2 h, and the usual oral dose is 30 to 60 mg to be taken 2 to 4 times a day. Thus nimodipine is a suitable candidate for oral controlled release drug delivery[40]. The natural gum based material successfully employed for formulating the controlled release matrix tablets of nimodipine. It is evident that the investigated controlled release matrix of Locust bean gum at 47% concentration was capable of prolonging the release of drug for 10 hrs.The mechanism of drug release was observed to be following Korsmeyer-Peppas model (Anomalous transport) and zero

order kinetics therefore both diffusion and erosion effect for controlled drug release[42]. Polymeric hydrophilic matrices are widely used for controlled-release preparations. The process of drug release is controlled by matrix swelling or polymer dissolution. It has been shown that the swelling of guar gum is affected by concentration of drug and viscosity grade of the polymer. This study examines the mechanism of behavior of guar gum in a polymer-drug matrix. The swelling action of guar gum, in turn, is controlled by the rate of water uptake into the matrices. An inverse relationship exists between the drug concentration in the gel and matrix swelling. This implies that guar gum swelling is one of the factors affecting drug release. The swelling behavior of guar gum is therefore useful in predicting drug release[24]. In a study on guar gum for the preparation of sustained release tablets [25], release data were found to be best fitted with the Higuchi release kinetics (The release kinetics have not been studied in that article, but the release data are available). Another study on guar gum matrix tablets containing metoprolol has shown that metoprolol tartrate release from guar gum matrices followed Fickian diffusion. When the hydrophilic guar gum tablets come into contact with the dissolution medium, they take up water and swell, forming a viscous gel barrier. In case of guar gum matrix tablets, the initial swelling of the gum may aid dissolution of the drug, and the dissolved drug diffuses out of the swollen gel barrier into the dissolution medium. Unless the swollen gel barrier erodes, further seeping-in of the dissolution medium does not occur. Thus, the release rate of the drug depends on the strength of the gel barrier (i.e. the proportion of the hydrophilic guar gum in the matrix tablet), its rate of hydration and viscosity [26].

Locust bean gum, **a** non starch polysaccharide consisting of galactose and mannose in the ratio 1:4 and hence they are known as galactomanan[9].The mannose elements form a linear chain linked with galactopyranosyl residues as side chain at varying distances depending on the plant origin[27]. Being a galactomanan locust Bean Gum has a wide application in pharmaceutical field. It is also known as Carob bean gum and is derived from the seeds of the leguminous plant *Ceratonia siliqua* Linn belonging to the family Fabaceae. This gum is widely cultivated in the Mediterranean region and to smaller extent also in California. The brown pods or beans of the locust bean tree are processed by milling the endosperms to form locust bean gum[28].

One of the most important goals of carboxymethylation of locust bean gum is to obtain water soluble derivatives. This modified gum can be used typically in pharmaceutical purposes as rate controlling polymer. They behave as a typical polyelectrolyte[5].

Assam Bora can be a promising option for mucoadhesive controlled drug delivery systems as natural substance[29].

The ratio of drug and polymer plays an important role in overall release of the drug and the formulated gum olibanum matrix tablets with drug: polymer 1:1.5 offered comparative release profile with that of marketed formulation.[43]

Diclofenac release from the matrix tablets formulated was slow and spread over 24 h and depended on the concentration (%) of olibanum resin in the matrix tablets and nature/type of diluent. As the concentration of olibanum resin in the matrix tablets was increased, drug release was decreased. Release was relatively faster with water soluble diluent lactose when compared to water insoluble diluent DCP at all concentrations of olibanum resin.

Drug release from the tablets followed first order kinetics and followed non - Fickian (anomalous) diffusion release mechanism. Good linear relationships were observed between percent polymer and release rate in each case. The results of the study thus indicated olibanum resin could be used as rate controlling matrix in design of controlled release tablets. Both water soluble and water insoluble diluents can be included in the olibanum resin matrix tablets without affecting its rate controlling efficiency. Matrix tablets formulated employing olibanum resin (DF2) are considered suitable for controlled release of diclofenac over 24 h (i.e. once-a-day administration)[44]. The matrix building material with fast polymer hydration capability is the best choice to use in a hydrophilic matrix tablet formulation. An inadequate polymer hydration rate may

cause premature diffusion of the drug and disintegration of the tablet owing to fast penetration of water. It is particularly true for formulation of water soluble drug. The polymers used in the preparation of hydrophilic matrices are divided into three broad groups as follow,

1) Cellulose derivatives

Hydroxyethylcellulose,

Hydroxypropylmethylcellulose (HPMC) 25, 100,4000 and 15000 cps, Sodium

carboxymethylcellulose and Methylcellulose 400and 4000 cps.

Non-cellulose natural or semisynthetic polymers Agar-agar, Carob Gum, Alginates,Molasses, Polysaccharides of mannose and Galactose, Chitosan and Modified starches.

Polymers of acrylic acid Polymers which are used in acrylic acid category are Carbopol 934. Other hydrophilic materials used for preparation of matrix tablet are Alginic acid, Gelatin and Natural gums[30].

The formulated matrix tablets of Furosemide met the pharmacopoeial requirement of uniformity of weight. All the tablets conformed to the requirement of assay, as per I.P. Hardness, percentage friability and thickness was all within acceptable limits.

There are several bioadhesive polymers now available with varying degree of mucoadhesive which is used in formulation of different dosage form. Some given in table -1.

Polymer	**Origin**	**Charge**	**Solubility in water**	**Mucoadhesive capacity**
Sodium alginate	Natural	Anionic	Soluble	++(+)
Hyaluronans	Natural	Anionic	Soluble	+++
Sodium CMC	Natural	Anionic	Soluble	++(+)
Poly (galacturronic) Acid	Natural	Anionic	Insoluble	+++
Xyloglucan	Natural	Anionic	Soluble	+
Pectin	Natural	Anionic	Soluble	++(+)
Xanthan gum	Natural	Anionic	Soluble	+
Methyl cellulose	Natural	Nonionic	Soluble	+
Chitosan	Natural	Cationic	Soluble	++

Table 1: There are several bioadhesive polymers now available with varying degree of mucoadhesive [[32, 33, 34, 35, 36], and [37]].

In above table 1 shows; Mucoadhesive capacity: +++: excellent; ++: good; +: Poor/absent.

The slow and sustained release of Trimetazidine dihydrochloride over a period of 12 hours was obtained by using Xanthan gum.[46]

Matrix tablets were prepared by wet granulation method and were evaluated for weight variation, content uniformity, friability, hardness, thickness, swelling index, in vitro dissolution, and stereo photography. Among the formulations studied, formulation containing combination of KG and XG (2:8) having concentration of 20% showed sustained release

of drug for 12hrs with cumulative percent release of 99.24%. The kinetic treatment showed that the optimized formulation follow zero order kinetic with release exponent (n) 0.7656 and having good stability as per ICH guidelines. No chemical interaction between drug and gums was seen as confirmed by IR studies. The matrix formulation showed sustained release of Metotprolol succinate by the diffusion mechanism.[47] An addition of anionic gaur gum into cationic chitosan tablet as matrix component could prolong the drug release greater than that containing single polymer.[48]

Microspheres using natural polymers:

A higher concentration of polymer produced a more viscous dispersion, which formed larger droplets and consequently larger microspheres. The higher concentration of polymer (more than 0.75 %) leads to irregular shape of microspheres was observed. The drug entrapment efficiency of Xanthan gum microspheres was found to be more then Guar gum microspheres. As compare to Guar gum, Xanthan gum is release retardant as guar gum showed 80.4% release whereas xanthan gum showed 78.9% release after 8 hrs. Guar gum and Xanthan gum are natural polymers that has been used frequently in colon targeting as carriers because of their safety, effectiveness, cost and availability.[49]

Conclusion

Natural gums are in general strong, low cost, reproducible and biocompatible, so they can be tailored for pharmaceutical applications. Natural polymer derivatives are often used to modify the release of drugs in tablet and capsule formulations and also as tablet binding, thickening and rheology control agents, for film formation, water retention, improving adhesive strength, for suspending and emulsifying. In light of the aforementioned discussion, it could be concluded that natural gums can be used as an effective controlled release polymers to retard the release of formulation for extended period of time. Several polymers from plant origin have been successfully used and others are being investigated as excipients in the design of dosage forms for effective sustained release drug delivery.

References

1. Kulkarni GT, Gowthamarajan K, Brahamajirao, Suresh B. Evaluation of binding properties of selected natural mucilages. J Sci Ind Res. 2002; 61: 529-32.
2. Shankaracharyan B. Tamarind-Chemistry, technology and uses: A critical appraisal. J Food Sci Technol. 1998; 35(3): 193-208.
3. Jaganath, et al: Preparation of silymarin control release tablets using natural gums,ijpsn,vol.4,issue:I june 2011.

4. Vajpyee et. al/ Formulation and Evaluation of Colon Targeted Curcumin Microspheres Using Natural Polymers: Jpro, 1: 4 (2011) 108 – 112.

5. Dey et al/carboxymethyl ethers of locust bean gum: a review, int j pharm pharm sci, vol 3, issue 2, 2011, 47.

6. Bhardwaj TR, Kanwar M, Lal R, Gupta A. Natural Gums and modified natural gums as sustained release carriers. Drug Deliv and Indus Pharm 2000; 26:1025-1038.

7. Sultzbaugh KJ, Speaker TJJ. A method to attach lectins to the surface of spermine alginate microparticles based on the avidin biotin interaction. J of Microencap 1996; 13(4):363-375.

8. Quong D, Neufeld RJ.DNA encapsulation within co-guanidine membrane coated alginate beads and protection from extracapsular nuclease. J of Microencap 1999; 16(5):573-585.

9. Maiti S, Dey P, Banik A, Sa B, Ray S, Kaity S. Tailoring of locust bean gum and development of hydrogel beads for controlled oral delivery of glipizide. Drug Deliv 2010; 17(5): 288-300.

10. Kumar *et al*. International Journal of Drug Delivery 2 (2010) 58-63.

11. Gilhotra Ritu Mehra et al. Enhancement of miotic potential of pilocarpine by tamarind gum based *in-situ* gelling ocular dosage form. Acta Pharmaceutica Sciencia 52: 145-154 (2010)

12. Glicksman, M. (1986). Tamarind seed gum in food hydrocolloids. Florida CRC Press, 3: 191.

13. Khanna, M., Nandi, R.C. and Sarin, J.P. (1997). Standardization of Tamarind seed powder for pharmaceutical use. Ind. Drugs 24: 268.

14. Liu, Z., Li, J., Nie, S., Liu, H., Ding, P. and Pan, W. (2006). A study of alginate/HPMC-based in situ gelling ophthalmic delivery system for gatifloxacin. Int. J. Pharm. 315: 12.

15. Cohen, S., Lobel, E., Trevgoda, A. and Peled, Y. (1997) A novel in situ forming ophthalmic drug delivery system from alginates undergoing gelation in the eye. J. Control. Rel. 44: 201.

16.Rashmi, Topical Gel : A Review,pharmainfo.net **05/08/2008 - 17:31.**

17. Gupta V, Puri R, Gupta S, Jain S, Rao GK. Tamarind kernel gum: An upcoming natural polysaccharide. Syst Rev Pharm 2010;1:50-4

18. Dumitriu S., Vidal P.F. and Chornet E. Hydrogels based on polysaccharides. In: Dumitriu S., Editor. Polysaccharides in medical applications. Marcel Dekker Inc, 1996, 125–242.

19. Miyazaki S. and Kawasaki N. Comparison of in situ gelling formulations for the oral delivery of cimetidine. Int. J. Pharm., 2001, 220:161–168.

20. Miyazaki S., Hirotatsu A., Kawasaki N., Wataru K. and Attwood D. In situ gelling gellan formulations as vehicles for oral drug delivery. J. Control Rel., 1999, 60:287–295.

21. Sechoy O., Tissie G., Sebastian C., Maurin F., Driot J.Y. and Trinquand C. A new long acting ophthalmic formulation of carteolol containing Alginic acid. Int. J. Pharm., 2000, 207:109–116.

22. Al-Shamklani A., Bhakoo M., Tuboku M.A. and Duncan R. Evaluation of the biological properties of alginates and gellan and xanthan gum. Proc. Int. Symp. Control Release Bioact. Mater., 1991, 18:213–217.

23. Praveen kulhar et al Evaluation of Guar Gum in the Preparation of Sustained-Release Matrix Tablets informa healthcare 1998, Vol. 24, No. 11 , Pages 1095-1099.

24. Jaber Emami*,et al. Preparation and In Vitro Evaluation of Sustained-Release Matrix Tablets of Flutamide Using Synthetic and Naturally Occurring Polymers, Iranian Journal of Pharmaceutical Research (2008), 7 (4): 247-257.

25. Khullar P, Khar RK and Agarwal SP. Evaluation of guar gum in the preparation of sustained-release matrix tablets. Drug Dev. Ind. Pharm. (1998) 24: 1095-1099

26. Krishnaiah YSR, Karthikeyan RS and Satyanarayana V. A three-layer guar gum matrix tablet for oral controlled delivery of highly soluble metoprolol tartrate. Int. J. Pharm. (2002) 241: 353-366.

27. Sharma BR, Dhuldhoya NC, Merchant SN. Glimpses of Galactomannans. Sci Tech Entrepreneur 2008; 3: 1-10.

28. Beneke CE, Viljeon AM, Hamman JH. Polymeric plant derived excipients in drug delivery. Molecule 2009; 14:2602-2620.

29. Sachan & Bhattacharya Drug Release from Glutinous Rice StarchInt J Health Res, March 2009; 2(1): 94.

30. Shalin A. Modi sustained release drug delivery system : a reviewijprd/2011/pub/arti/vov-2/issue-12/feb/016 .

31. Sourabh Jain Preparation and Evaluation of Sustained Release Matrix Tablet of Furosemide using Natural Polymers Research J. Pharm. and Tech. 1(4): Oct.-Dec. 2008;Page 374-376.

32. Andrews GP, Laverty TP and Jones DS: Mucoadhesive polymeric platforms for controlled drug delivery Review article. European Journal of Pharmaceutics and Biopharmaceutics 2009; 71: 505–518.

33. Lehr CM, Bouwstra JA, Schacht EH and Junginger HE: In vitro evaluation of mucoadhesive properties of chitosan and some other natural polymers. Inernational. Journal Pharmceutics 1992; 78: 43–48.

34. Ludwig A: The use of mucoadhesive polymers in ocular drug delivery. Advanced Drug Delivery Reviews 2005; 57: 1595– 1639.

35. Patil SB, Murthy RSR, Mahajan HS, Wagh RD and Gattani SG. Mucoadhesive polymers: Means of improving drug delivery. Pharma Times 2006:38: 25-28.

36. Vasant V. Ronade, Mannfred A. Hallonger: intranasal and ocular Drug delivery system, CRC press pharmacology press, second edition, 2008, 267-280.

37. Uchegba IF and schtzeil AG: Polymer in drug delivery. Taylor and francis group
2007, 163-183.

38. Dhopeshwarkar V,Zatz JL,Evaluation of Xanthan gum in the preparation of sustain release matrix tablets.Drug Dev.Ind.Pharm.1993 ;19(9):999-1017

39 Yeole PG,Babla IB,Nakhat PD,Design and evaluation of Xanthan gum based sustain release matrix tablet of d i c l o f e n a c s o d i u a m . I n d i a n J.Pharm.Sci.2006; 68(2):185-189.

40. Rajendran A, Basu SK. Alginate-Chitosan Particulate System for Sustained Release of Nimodipine. Tropical Journal of Pharmaceutical Research, October 2009;8 (5): 433-440

41. Choudary KPR,Mohapatra P.Evaluation of olibanum and its resin as rate controlling matrix for controlled release of diclofenac. Indian J.Pharm.Sci.2006; 68(4):497-500.

42. Bangale G.S *et al* Formulation and Evaluation of Natural Gum Based Matrix Tablets for Oral Controlled Delivery of Nimodipine. nd J Pharm Edu Res, Oct-Dec, 2011/ Vol 45/ Issue 4.

43. Muzib et al. Int J Pharm Pharm Sci, Vol 3, Issue 2, 2011, 195199.

44. Chowdary and Reddy, formulation and evaluation of diclofenac controlled release tablets employing olibanum resin ijpsr, 2012; vol. 3(4): 1090-1095.

45. N.ahuja et al, formulation and evaluation of diclofenac sodium gel by using natural polymer.

46. H.Sankhala,et al ,formulation and evaluation of sustained release tablet of Trimetazidine Dihydrochloride, Ijppr, Volume 2, Issue2, April 2011.

47. V. N. Deshmukh et al. Formulation and Evaluation of Sustained Release Metoprolol Succinate Tablet using Hydrophilic gums as Release modifiers /Int.J. PharmTech Res.2009, 1(2)

48. Shanker S.j. formulation and evaluation of controlled release matrix tablets of an antimicrobial drug ijprd/2010/pub/arti/vov-2/issue-10/dec/002.

49. Vajpyee et. al/ Formulation and Evaluation of Colon Targeted Curcumin Microspheres Using Natural Polymers, Journal of Pharmaceutical Research And Opinion 1: 4 (2011) 108 – 112.

Correspondence Address:

D.K.Gupta*

Asst. Prof.

Dept. of Pharmacy, B.I.T, Meerut, U.P,

INDIA.

Email: *dineshgupta_008@rediffmail.com*