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Review on Application of Xanthan Gum in Drug Delivery

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Abstract: Xanthan gum is a commercially important polysaccharide that has immense applications in diverse fields due to its unique rheological properties. They are used in food industries, pharmaceutical industries, agricultural industries, textile industries etc. This particular exopolysaccharide is produced by *Xanthomonas campestris* bacteria utilising glucose as the major carbon source. Xanthan gum has been preferred in pharmaceutical formulations as a gelling agent, binder and disintegrant. Controlled drug release is essential in order to increase the efficacy of the drug delivery to the target region without causing a toxic effect. Xanthan gum has the potential in retarding drug release to its gelling nature and ability of entrapping the drug within the gel. In this review, use of xanthan gum in various drug delivery systems has been discussed.
Keywords: Xanthan gum, Drug delivery, exopolysaccharides, Liposomes, Hydrogel, Matrix Systems, Niosomes, Microspheres.

Introduction

Xanthan gum is an extracellular bacterial exopolysaccharide synthesized by *Xanthomonas campestris*. The unique properties of xanthan gum make it versatile to be used in different applications. They are highly soluble in water, stable over a wide range of temperature, acidic and alkaline conditions. It is resistant to enzymatic degradation and also exhibits synergistic interactions with other hydrocolloids. Xanthan gum is produced by natural microbial fermentation process which converts glucose to produce this product of economic importance. Xanthan gum is an acidic polymer with repeating pentasaccharide units having two glucose units, two mannose units and one glucuronic acid unit in the ratio of 2.8:2.0:2.0 (1). The xanthan gum is anoinic in nature due to pyruvic acid and glucuronic acid groups in the side chains. Due to high production cost of carbon source, many low cost substrates were utilized for xanthan gum production (2). Natural gums are generally preferred over synthetic gums because they are non-toxic, more biocompatible, cheap, easily degradable and the scope of availability is also more. There is a safety concern with respect to the usage of natural gums in pharmaceutical industry which increases the strict evaluation of the product quality which only few natural gums can fulfil. The various gums that are being used extensively in pharmaceutical industry are alginate, chitosan, carrageenan, gellan gum, xanthan gum, guar gum, gelatine etc (3). The properties that enable the application of xanthan gum in pharmaceutical industries are emulsifying, thickening, stabilising, film forming and gelling nature (4). Xanthan gum is already a widely used product in the market when compared to the other polysaccharides of plant and microbial origin and it has already been accepted by the US food and drug administration in 1969 and received European Union approval under the E- number 415 in 1980. The rheological properties of xanthan gum and its uniqueness compared to other gums render it to be used in other industries such as oil, paper, agricultural, textile, paint, cosmetic industries etc. Even though the polysaccharides of plant origin are less expensive than microbial polysaccharides, the one advantage of

microbial polysaccharides is that better product quality can be ensured during the production incompatible with it such as Amitriptyline, Tamoxifen, Verampil (5).

Poysaccharide Drug Delivery Systems

Controlled release of drug delivery is essential in order to increase the effectiveness of drug therapy. This also reduce the chance of toxic condition caused by rapid drug level in the plasma and can also avoid repeated administration of drug (6).Targeted drug delivery system is highly recommended for colon associated diseases namely colitis ulcerosa, Crohn syndrome, amebiosis, colorectal adenocarcinoma, general delivery of protein and peptide drugs. This type of drug delivery system ensures more bioavailability of drug to the targeted area and prevents the loss of drug as there is a chance of release or absorption in the stomach and the degradation of the active ingredient (7). They also function as taste masking, stabilising agent, protective and rate controlling agent (8). Oral route of administration is the most preferred one but the probability of drug release before reaching the target site gives it a second thought to be preferred. In order to have a targeted release of the active ingredient, a controlled release is to be achieved which can be obtained using some controlled release mechanisms. Some natural polysaccharides such as guar gum, xylan gum and xanthan gum are only selectively degraded in the colon not in stomach and in small intestine(9). So employing these polysaccharides in colon drug delivery provides a better option for treating colon associated diseases. In general diffusion was adapted for soluble drugs and erosion was adapted for sparingly soluble or insoluble drugs through erosion (10). Ramasamy et al indicates the erosion ratio of the tablets containing xanthan gum and aclofenac, it was found that with increasing ratio of polymer in the tablet the erosion also increased and the tablets with increasing concentration of xanthan gum were releasing only less drug in stomach and in intestinal medium when compared to tablets with less amount of xanthan gum. Large amount of polymer in the formulation increases the swelling which is related to the intake of large amount of water and formation of viscoelastic mass (11). In order to achieve high drug profile and controlled release matrix systems are developed with hydrophilic polymeric systems (12). Xanthan gum is used in gum based sustained release tablet and provides time independent release kinetics (13). It has been estimated as a controlled release formulation for theophyllline, Aclofenac (10), Metronidazole (14), Furosemide (15), Isosorbide-5-mononitrate (12) and Indomethacin (16). Sourabh Jain et al. observed that cumulative drug release percent decreases with increasing gum concentration and swelling index. In one of the experiments, it was also found out that xanthan gum showed higher ability to retard the drug release than synthetic hydroxypropyl methyl cellulose (17).

Drug delivery to the targeted sites is almost impossible without the help of a suitable potential carrier that can deliver the drug to the site of pharmacological action without wasting the active ingredient. The carriers are chosen which are biodegradable and can be naturally excreted from the body, these polymers can be excreted directly by the kidney or can be degraded in to smaller molecules and can be excreted. Drug delivery carriers include liposomes, hydrogels, nanoparticles, microspheres, nanofibres, dendrimers etc. This review paper focuses on investigating the application of xanthan gum in different drug carrier systems and its efficacy in targeted drug delivery.

Liposomes

Liposomes are artificially prepared spherical vehicles made of lipid bilayer which can be used for delivery of both hydrophobic and hydrophilic compounds and can avoid the degradation of entrapped compounds, releasing it on the targeted sites. The liposome contents are protected from enzymes, free radicals, digestive juices with the help of lipophillic barrier around the contents (18). But the stability of liposomes in solution is sometimes affected which can be overcome by the usage of suitable polymers. Chitosan is a polymer that is used in increasing vesicle stability, in a particular study xanthan gum, a poly anionic compound is allowed to undergo macromolecular complexation with polycationic compound chitosan and is studied for its effectiveness in increasing the vesicle stability synergistically. It was found that liposomal formulation for pulmonary delivery was found to have a positive effect by the liposome coating with polyelectrolyte complex formed of xanthan gum and chitosan (19).

Hydrogel

Hydrogels are network of hydrophilic polymeric network chains which resemble much like a biological tissue in imbibing large amount of water. They can be formulated in a variety of physical forms such as films, slabs, coatings, gels etc. Porosity of a hydrogel is an important factor that determines the drug loading capacity as well as the subsequent release of drug which can be controlled by using cross linking agents and the concentration of polymers (20). Swelling of hydrogels are determined by factors such as the cross linking ratio and the chemical structure of the polymer. Swelling kinetics of hydrogel include diffusion controlled and

relaxation controlled, called as Fickian and Non-Fickian respectively (21). Superporous hydrogels are hydrophilic polymers that are cross linked very lightly in order to enhance the swelling and absorption ability to a higher extent. Through permeation and by capillary action rapid absorption of water takes place in the macromolecular structure. Sunny Gils et al. have mentioned the synthesis of super porous hydrogels, using xanthan gum, 2 hydroxyethylmethacrylate and acrylic acid by free radical graft polymerisation method (22). It was observed that xanthan gum does not form hydrogels readily but are only formed when the aqueous solutions are annealed to a particular temperature and cooled suddenly (23).

Matrix Systems

Biopolymeric matrix systems are used in the controlled release of active drug ingredients Matrix systems are made of polymeric materials that are swellable in the presence of water or biological fluids. In this the powdered drug is distributed uniformly in a matrix of polymeric material and they are compressed to form a tablet. The dissolved or the dispersed drug undergoes a controlled drug release pattern. Mundargi et al. reported that in xanthan grafted co-polymer of acrylamide, the release rate increased with increasing the graft ratio (24). Depending on drug charges hydrogel exhibited selective permeability which helps in the controlled release of formulation (25). These gums find use as binders and disintegrants in tablets. The swelling property of these polymers helps in the disintegration of tablets and improves the dissolution rate of drug. In a particular study it was reported that xanthan gum mediated drug release in sustained release mini matrices developed by hot melt extrusion method exhibited high swelling and erosion rate, faster drug release, high absorption rate (26). Amir et al. have experimentally proved that in matrix tablets formulation using xanthan gum, guar gum, k-carrageenan and xanthan gum. k-carrageenan showed high swelling of matrices and also retarded the release of drug release more than guar gum (27).In another study related to colon targeted drug release, matrix tablets of albendazole was prepared using xanthan gum and it was found that the rate of drug release was decreased with increasing xanthan gum concentration but a profound increase in the drug release rate was found when in vitro drug release study was conducted in the rat cecal content which indicates the presence of polymer degrading enzymes are present in the rat cecal content (39). Jackson et al. reported that when xanthan gum and ethyl cellulose were used in matrix tablets used in colon drug delivery, higher concentration of xanthan gum exhibited more drug retarding capability than the formulation with ethyl cellulose (14).

Niosomes

Niosomes are an emerging drug carrier transport system which is vesicular type almost similar to liposome in structure but superior to liposomes in stability and they are cheap. They contain hydrophilic and hydrophobic region where both hydrophobic and hydrophilic drugs can be incorporated and delivered to the targeted sites. They are used in ophthalmic drug delivery, acts as carriers for haemoglobin and peptide drugs, diagnostic agents etc (28). Shinde et al. reported that when xanthan gum was used in the preparation of niosomes there was change in the particle size, good spreadability was also observed compared to the formulation without using xanthan gum and the niosomal formulation exhibited pseudoplastic behaviour. Physical stability was also found to be more in xanthan gum containing formulation, and even though at higher temperature there is chance of enzyme leakage from gels, it was found that it was less when the niosomal formulation is converted to gel with the help of xanthan gum. Thus it was experimentally proved that xanthan gum can be used as a gelling agent in the preparation of serratiopeptidase noisome gel (29).

Nanoparticles

Nanoparticles help in cell specific targeting by attaching drug molecules to the designed carriers. They adsorb or encapsulate or entrap the drug molecule protecting it from degradation and exhibit distinct physicochemical and biological properties that makes it suitable for drug delivery applications. The small size of nanoparticles ranging from 1 to 100 nm helps them to be easily absorbed than the larger molecules. The advantage of nanoparticles over liposomes is that the surface characteristics and the particle size can be efficiently manipulated in these systems (30). Polysaccharide nanoparticles can be synthesised by means of covalent cross linking, ionic cross linking, poly electrolyte complexation etc., (31). Pooja et al. investigated on the usage of xanthan gum as reducing agent in the synthesis of gold nanoparticles. These nanoparticles are involved in drug delivery because of their size and efficient targeted drug release. It was found that the gold Nan particle synthesised using xanthan gum was non-toxic and biocompatible in the hemolysis study. They also showed high drug loading, stability and enhanced cytotoxicity in lung cancer cells (32). In a study it was also reported that the viscoelastic gel formed by the synergistic interaction of xanthan gum and guar gum mixtures can lead to the stabilisation of micro and nano scale iron particles (33).

Microspheres

Microspheres are small spherical particles ranging in size from 1 to 1000 µm that are used in the controlled delivery of unstable drugs. They are found to be used in gene delivery, oral drug delivery, nasal drug delivery, gastro intestinal drug delivery and are also exploited in various other routes of drug administration (34). They help in the oral controlled drug release using hydrophilic polymers in multiple dosage forms which aids in the uniform and prolonged release of drug. Bhattacharya et al. reported that xanthan gum and polyvinyl alcohol when cross linked, a three dimensional interpenetrating polymer network is formed, it exhibited as a potential candidate in delivering drug in a much sustained released pattern. The drug release followed a non-Fickian mode of drug release (13). In a study conducted by Deshmukh et al. it was reported that when hydrophilic gums such as xanthan gum and locust bean gum were used, it helped in retarding the drug release and extending the drug release time in microspheres of calcium alginate formed by ionotropic gelation method. It was observed that the drug entrapment efficiency with increase in the concentration of hydrophilic polymers. The steps involved in the release of drug release from polymer drug matrix are penetration of solvent in to the matrix, polymer gelation, drug dissolution and diffusion of drug through the different layers (35).

Conclusion

Different drug carrier systems was developed in order to improve efficacy in drug delivery system so that degradation of drug during transport, toxic effects due to rapid release can be avoided and better drug transport to the target sites can be achieved. This also helps in reducing the side effects associated with conventional drug delivery techniques. In all the above discussed formulations controlled release, biocompatibility and biodegradability was observed which makes it convenient to be used in pharmacological applications. Thus targeted delivery aids not only in maintaining the therapeutic benefits but also in avoiding the overall toxic effects associated with the conventional approaches.

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References

1. Becker A., Katzen F., Puhler A. and Ielpi L., Xanthan gum biosynthesis and application: a biochemical/genetic perspective, Appl. Microbiol. Biotechnol., 1998, 50, 145–152.
2. Gunasekar, V., Reshma, K. R., Treesa, G., Gowdhaman, D., and Ponnusami, V, Xanthan from sulphuric acid treated tapioca pulp: Influence of acid concentration on xanthan fermentation, Carbohydr. Polym., 2104, 102, 669– 673.
3. Jana S., Gandhi A., Sen K.K. and Basu S. K., Natural Polymers and their Application in Drug Delivery and Biomedical Field, J. PharmaSci Tech., 2011, 1, 16–27.
4. Jani G.K., Shah D.P., Prajapati V.D. and Jain V.C., Gums and mucilages : versatile excipients for pharmaceutical formulations, Asian J. Pharm. Sci., 2009, 4, 308–322.
5. Shanmugam S., Manavalan R., Venkappayya D., Sundaramoorthy K., Mounnissamy VM., Hemalatha S. and Ayyappan, T., Natural polymers and their applications, 2005, 4, 478-481.
6. Gothoskar A. V., Anagha M. J., and Nitin H. J., Pulsatile drug delivery systems: a review, Drug delivery tech., 2004, 4, 1-11.
7. Philip A. K. and Philip B., Colon targeted drug delivery systems: a review on primary and novel approaches, Oman Med. J., 2010, 25, 79–87.
8. Kola R and Kumar B.P., A Detailed Description Of Synthetic And Natural Polymers Which Are Used In The Formulation Of Sustained Release Drug Delivery System : A Review, J. Chem. Pharm. Sci., 2013, 6, 161–9.
9. Salyers A.A., Vercellotti J.R., West S.E.H. and Wilkins TD., Fermentation of mucin and plant polysaccharides by strains of Bacteroides from the human colon, Appl. Environ. Microbiol., 1977, 33, 319–22.
10. Ramasamy T., Devi U., Kandhasami S. and Ruttala H., Formulation and evaluation of xanthan gum based aceclofenac tablets for colon targeted drug delivery, Brazilian J. Pharm. Sci., 2011, 47, 299–311.
11. Talukdar M.M. and Kinget R., Swelling and drug release behaviour of xanthan gum matrix tablets, Int. J. Pharm., 1995, 120, 63–72.

12. Kar R., Mohapatra S., Bhanja S., Das D. and Barik B., Formulation and In vitro characterization of xanthan gum-based sustained release matrix tables of isosorbide-5- mononitrate, Iran. J. Pharm. Res., 2010, 9, 13–19.
13. Bhattacharya S.S., Mazahir F., Banerjee S., Verma A. and Ghosh A., Preparation and in vitro evaluation of xanthan gum facilitated superabsorbent polymeric microspheres, Carbohydr. Polym., 2013, 98, 64–72.
14. Jackson, C., and Ofoefule, S., Use of Xanthan Gum and Ethylcellulose in Formulation of Metronidazole for Colon Delivery, J. Chem. Pharm. Res., 2011, 3, 11–20.
15. Jain S., Yadav SK. and Patil UK, Preparation and Evaluation of Sustained Release Matrix Tablet of Furosemide using Natural Polymers, Res. J. Pharm. Tec., 2008, 1, 374–376.
16. Asghar L.F., Chure C.B. and Chandran S., Colon specific delivery of indomethacin: effect of incorporating pH sensitive polymers in xanthan gum matrix bases, AAPS PharmSciTech., 2009, 10, 418–29.
17. Vishakha K., Kishor B. and Sudha R., Natural Polymers – A Comprehensive Review, Int. J. Res. Pharm. Biomed. Sci., 2012, 3, 1597–1613.
18. Akbarzadeh A., Rezaei-Sadabady R., Davaran S., Joo SW., Zarghami N. and Hanifehpour Y., Liposome: classification, preparation, and applications, Nanoscale Res. Lett., 2013, 8, 1–9.
19. Manca M.L., Manconi M., Valenti D., Lai F., Loy G. and Matricardi P., Liposomes Coated with Chitosan – Xanthan Gum (Chitosomes) as Potential Carriers for Pulmonary Delivery of Rifampicin, J. Pharm. Sci. 2011;1–10.
20. Bindu Sri., Ashok V. As A Review on Hydrogels as Drug Delivery in the Pharmaceutical Field. Int. J. Pharm. Chem. Sci. 2012;1(2), 642–661.
21. Peppas, N. A., Bures, P., Leobandung, W., and Ichikawa, H., Hydrogels in pharmaceutical formulations. Eur. J. Pharm. Biopharm. 2000, 50, 27–46.
22. Gils P.S., Ray D. and Sahoo P.K., Characteristics of xanthan gum-based biodegradable superporous hydrogel, Int. J. Biol. Macromol., 2009, 45, 364–371.
23. Iijima M., Shinozaki M., Hatakeyama T., Takahashi M. and Hatakeyama H. AFM studies on gelation mechanism of xanthan gum hydrogels. Carbohydr. Polym. 2007, 68, 701–707.
24. Mundargi R.C., Patil S.A., Aminabhavi T.M., Evaluation of acrylamide-grafted-xanthan gum copolymer matrix tablets for oral controlled delivery of antihypertensive drugs. Carbohydr. Polym., 2007, 69, 130–41.
25. Shalviri A., Liu Q., Abdekhodaie M.J. and Wu X.Y., Novel modified starch–xanthan gum hydrogels for controlled drug delivery: Synthesis and characterization, Carbohydr. Polym., 2010, 79, 898–907.
26. Verhoeven E., Vervaet C. and Remon J.P., Xanthan gum to tailor drug release of sustained-release ethylcellulose mini-matrices prepared via hot-melt extrusion: in vitro and in vivo evaluation, Eur. J. Pharm. Biopharm., 2006, 63, 320–330.
27. Shaikh A., Shaikh P., Pawar Y. and Kumbhar S., Effect of gums and excipients on drug release of ambroxol Hcl sustained release matrices, J. Curr. Pharm. Res., 2011, 6, 11–15.
28. Ashutosh L., Suman R., Sidhyartha S., Altaf S. and Vandana YM. Review Article A Novel Drug Delivery System : Niosomes Review. J. Drug Deliv. Ther. 2012;2(5), 129–135.
29. Shinde U.A. and Kanojiya S.S. Serratiopeptidase Niosomal Gel with Potential in Topical Delivery. J. Pharm. 2014, 2014, 1–9.
30. Mohanraj V.J. and Chen Y., Nanoparticles – A Review. Trop. J. Pharm. Res. 2006, 5, 561–573.
31. Liu Z., Jiao Y., Wang Y., Zhou C. and Zhang Z. Polysaccharides-based nanoparticles as drug delivery systems. Adv. Drug Deliv. Rev., 2008, 60, 1650–1662.
32. Pooja D., Panyaram S., Kulhari H., Rachamalla SS. and Sistla R. Xanthan gum stabilized gold nanoparticles: Characterization, biocompatibility, stability and cytotoxicity. Carbohydr. Polym. 2014, 110, 1–9.
33. Xue D. and Sethi R. Viscoelastic gels of guar and xanthan gum mixtures provide long-term stabilization of iron micro- and nanoparticles. J. Nanoparticle Res., 2012, 14, 1239.
34. Sahil K., Akanksha M., Premjeet S., Bilandi A., Kapoor B. Microsphere: A Review. Int. J. Res. Pharm. Chem., 2011, 1, 1184–1198.
35. Deshmukh, V. N., Jadhav, J. K., Masirkar, V. J. and Sakarkar, D. M., Formulation, Optimization and Evaluation of Controlled Release Alginate Microspheres Using Synergy Gum Blends. Res. J. Pharm. Tec., 2009, 2, 324–327.

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