Innovare Academic Sciences

International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 6, Issue 10, 2014

Review Article

# MULTIPARTICULATE DRUG DELIVERY SYSTEMS USING NATURAL POLYMERS AS RELEASE RETARDANT MATERIALS

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*Received: 18 Jul 2014 Revised and Accepted: 25 Aug 2014*

**ABSTRACT**

Now-a-days, the emphasis of pharmaceutical researchers is turned towards the development of more efficacious drug delivery systems with already existing molecule. However, in recent applications, Multiparticulate drug delivery systems (MDDS) are gaining much favor over single- unit dosage forms because of their potential benefits like predictable gastric emptying, least risk of dose dumping, flexible release pattern and increased bioavailability with minimum inter- and intra- subject variability. The advances in such drug delivery systems have simultaneously urged the discovery of novel excipients which are safe and fulfill specific functions and directly or indirectly influence the rate and extent of release and/or absorption. The plant derived gums and mucilages comply with many requirements of pharmaceutical excipients as they are non-toxic, stable, easily available, associated with less regulatory issues as compared to their synthetic counterpart and inexpensive; also these can be easily modified to meet the specific need. The pharmaceutical scientists have achieved a great success in developing most therapeutic systems with suitable natural polymer. The current article focuses on the merits, limitations, types of MDDS and application of natural polymer as drug release retardant material for MDDS with supportive studies on natural polymer and MDDS currently available in the market.

**Keywords:** Multiparticulate drug delivery systems, Natural polymers, Drug release retardant materials, Gums, Mucilages, Polysaccharides.

## INTRODUCTION

Drug Delivery Systems (DDS) is a strategic tool for expanding markets/indications, extending product life cycles and generating opportunities. DDS make a significant contribution to global pharmaceutical sales through market segmentation, and are moving rapidly. Drug delivery systems are becoming increasingly sophisticated as pharmaceutical scientists acquire a better understanding of the physicochemical and biochemical parameters pertinent to their performance [1].

Despite of tremendous advancements in drug delivery, multiparticulate oral dosage forms acquired a centre stage in the arena of pharmaceutical research and development for achieving the delayed release oral formulations; thus provide tremendous opportunities and extending the frontier of future pharmaceutical development. These formulations release the drug at a time rather than promptly after administration, offers design flexibility and clinical benefits than single units such as short gastric residence time, most patient convenience means of drug administration, maximum drug absorption, reduce peak plasma fluctuations, minimize the potential side effects due to dose dumping and numerous technological, therapeutical advantages over single- unit forms [2]. Multiparticulate drug delivery systems (MDDS), mostly used for an oral route, consist of the multiplicity of small discrete units that exhibit different characteristics. Together, these characteristic units provide the overall desired controlled release of the dose. It is based on subunits such as granules, beads, microspheres, pellets, spheroids and Minitab. In MDDS, drug substances are divided into number of subunits, typically consist of thousands of spherical particles having diameter of about 0.05-2.00 mm. To administer or to recommend total dose these subunits are compressed into a tablet or filled into a sachet or encapsulated [3].

Multiparticulates may be prepared by several methods. Different methods require different processing conditions and produce multiparticulates of distinct qualities. Some of these methods may be broadly classified as pelletization, granulation, spray drying, and spray congealing. Drug particles may be entrapped within the multiparticulates or layered around them. Subsequently, these multiparticulates may be modified in many ways to achieve the desired drug release profile. One approach to the modification of drug release profile in multiparticulates is to coat them. Reasons for application of coating onto multiparticulates are to obtain functional coats, provide chemical stability, improve physical characteristics and enhance patient acceptance. Coats are formed from various polymeric coating materials broadly classified as aqueous polymer dispersions, polymer solutions, molten polymers and dry powders. Depending on the type of coating material used, functions such as sustained release (SR), targeted release, delayed release, and pulsatile release can be achieved [4].

### Merits of MDDS

This type of drug delivery has been at the centre of research due to its many benefits over conventional dosage forms, some of which are as follows:

- Predictable, reproducible and short gastric residence time
- Less inter- and intra-subject variability
- Improve bioavailability
- Reduced adverse effects and improved tolerability
- Limited risk of local irritation
- No risk of dose dumping
- Flexibility in design
- Ease of combining pellets with unlike compositions or release patterns
- Improve stability
- Improve patient comfort and compliance
- Achieve a unique release pattern
- Extend patent protection, globalize product and overcome competition[5].

### Limitations of MDDS

Multiparticulate drug delivery systems like other delivery systems have several limitations. These include

- Several formulation steps
- Higher cost of production
- Low drug loading
- Require advanced technology
- Proportionally higher need for excipients
- Lack of manufacturing reproducibility and efficacy
- Large number of process variables
- Trained/skilled individual needed for manufacturing [6].

**Types of MDDS**

There are different types of MDDS based on the drug release mechanism and these are enumerated and explained below.

I. Reservoir coated systems

II. Matrix coated systems

III. Specialized systems [7].

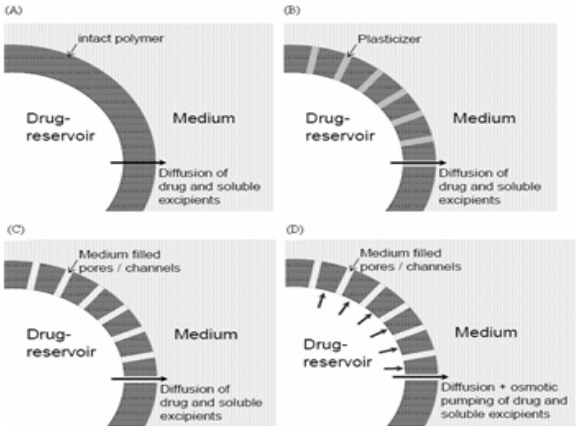


**Fig. 1: Schematic representation of typical release mechanism** [8]

**Reservoir coated systems**

Such systems consist of a drug layered core surrounded by a polymer. The mechanism of controlling the drug release from reservoir type systems is often complex and depends on coating type, thickness, drug type and core type. Those mechanisms include

- Diffusion through the continuous polymer film surrounding the drug loaded core. Firstly, water penetrates through the coating until reaches the pellet core. Afterwards, drug is dissolved and released due to the concentration gradient inside the pellet versus outside the pellet [Fig. 1(A)].

- Drug release can occur through water filled pores. These pores can be due to leaching of water soluble compounds into the release medium or due to cracks formed by high hydrostatic pressure generated inside these systems upon water uptake [Fig.1 (B & C)].

- For this mechanism to occur an osmotic active core is surrounded by semi-permeable membrane. Upon water uptake and under right circumstances, an osmotic pressure is built up within the interior of the core and the drug is pushed out via pores in the coating [Fig.1(C)] [9].

**Matrix coated systems**

In these systems a polymer: drug solution or dispersion is sprayed onto pellets in order to achieve controlled drug release. The drug and polymer are dissolved or dispersed in a common solvent and upon solvent evaporation, a solid solution (drug dissolved in the polymer) or a solid dispersion (drug dispersed in the polymer) or a combination of both is obtained. If the initial drug concentration is below drug solubility in the polymer, drug is dissolved and drug release is mainly controlled by drug diffusivity in the polymer [10].

**Specialized systems**

These MDDS can be specially designed into various types.

- **Pulsatile system based on rupturable coating**: This is a multiparticulate system in which the drug is coated onto the non-pareil sugar seeds followed by a swell able layer and an insoluble top layer. The release is independent of environmental factors like pH and drug solubility. The lag time can be varied by varying coating thickness or adding high amounts of lipophilic plasticizer in the outermost layer.

- **Low density floating multiparticulate pulsatile systems:** These systems reside only in the stomach and not affected by variability of pH local environment or gastric emptying rate. These are advantageous for drugs either absorbed from the stomach or requiring local delivery in stomach.

- **Time controlled expulsion systems:** This system is based on a combination of osmotic and swelling effects. The core contains the drug, a low density solid and/or liquid lipid material and a disintegrant. The core is further coated with cellulose acetate.

- **Sigmoidal release system:** This consists of pellet cores comprising drug and succinic acid coated with ammonia-methacrylate copolymer USP/NF type B. The time lag is controlled by the rate of water influx through the polymer membrane. The water dissolves acid and the drug in the core. The acid solution in turn increases permeability of the hydrated polymer film [11].

**Table 1: Examples of marketed MDDS** [12, 13]

| Product | Company | Drug | Release |
|---|---|---|---|
| Losec MUPS | AstraZeneca | Omeprazole magnesium | Delayed release multiple unit pellet system in tablet |
| Nexium | AstraZeneca | Esomeprazole magnesium | Enteric delayed release pellets in capsule |
| Toprol XL | AstraZeneca | Metaprolol succinate | Controlled release pellets in capsule |
| Avinza | King | Morphine sulfate | QD/IR+SR layered beads in capsule |
| SoluTab | Takeda | Lansoprazole | Delayed release enteric coated microgranules in tablet |
| Prevacid | Takeda | Lansoprazole | Delayed release enteric coated granules in capsule |
| Coreg CR | GSK | Carvedilol phosphate | QD/IR+SR polymer coated beads in capsule |
| InnoPran XL | GSK | Propranolol Hcl | QD / Delayed release SR coated beads in capsule |
| Spansule | GSK | d-amphetamine sulfate | QD/IR+SR coated beads in capsule |
| Focalin XR | Novartis | Dexmethylphenidate | QD / Bi-modal pulsatile release IR+Enteric delayed release beads in capsule |
| Adderall XL | Shire | Mixed salts of a single entity amphetamine | QD /double pulse drug layered and SR polymer coated beads |
| Carbatrol | Shire | Carbamazepine | BID / IR+SR+Enteric beads in capsule |
| Equetro ER | Validus | Carbamazepine | BID / IR+SR+Enteric beads in capsule |
| Metadate CD | UCD, Inc. | Methylphenidate | QD /30%IR + 70% SR coated beads |
| Pentasa | Shire | Mesalamine | Controlled release beads in capsule |
| Luvox CR | Jazz | Fluvoxamine maleate | QD / polymer coated beads in capsule |
| Amrix | Cephalon | Cyclobenzaprine Hcl | QD/ polymer coated beads in capsule |

**Natural polymers as release retarding material for MDDS**

Extensive applications of polymers in drug delivery have been realized because polymers offer unique properties which have not been attained by any other materials. Polymers have been successfully investigated and employed in the formulation of solid, liquid and semi-solid dosage forms and are specifically useful in the design of novel drug delivery systems. Pharmaceutical polymers are widely used to achieve taste masking; controlled release (e.g. extended, pulsatile and targeted) enhanced stability and improved bioavailability [14, 15]. Polymers which are used as release retarding materials in the design of sustained and controlled release drug delivery systems play a vital role in controlling the delivery of the drug from these systems. The success of modified drug delivery system depends on how well the polymer regulates the release of drug from the systems. Though a wide range of release retarding polymers are available, there is a continued need to develop new and more efficient release - retarding polymers for sustained and controlled release [16, 17].

Today, the whole world is increasingly interested in natural drugs and excipients. Continued improvement and accelerating research and development in polymeric materials has played a vital role in the progress of most controlled release technologies. In the past 25 years, there has been a considerable increase in interest in this technology, as is shown by the increasing number of publications and patents in the area of controlled drug-release systems using synthetic as well as naturally occurring polymeric materials [18]. Both synthetic and natural polymers have been investigated extensively for this purpose. Synthetic polymers are toxic, expensive, have environment related issues, need long development time for synthesis and are freely available in comparison to naturally available polymers. Ability to produce a wide range of material based on their properties and molecular weight. Natural polymers became a thrust area in the majority of investigations in drug [19].

With the availability of variety of natural polymers, the manufacturers today have a great success in developing the most promising therapeutic systems, namely drug delivery system, which provides an effective therapy to patients for prolonged periods [20]. The release behavior of drug from the formulation containing natural polymers depends on the physicochemical properties of both the drug and polymer. Release pattern of polymer, morphology, particle size, size and shape of dosage form are some of factors that influence the release of drug. Natural polymers, gums and mucilages modify the drug release from formulation [21].

Natural gums and mucilages are preferred over semi-synthetic and synthetic excipients in the field of drug delivery because they are cheap and easily available, have soothing action and nonirritant nature. Further, they are eco-friendly, capable of multitude of chemical modifications, potentially degradable and compatible due to their natural origin [22]. It should be noted that many “old” materials compete successfully today after almost a century of efforts to replace them. It is the usual balance of economics and performance that determines the commercial realities. Natural gums are among the most popular hydrophilic polymers because of their cost effectiveness and regulatory acceptance [23]. Natural gums have been modified to overcome certain drawbacks like uncontrolled rate of hydration, thickening, drop in viscosity on storage, microbial contamination etc [24]. Different natural gums have been used to design oral controlled release multi particulate dosage forms such as microspheres are becoming more popular single unit dosage forms [25]. In several cases, the polysaccharides, resins or the tannins present in the gum are responsible for imparting release retardant properties to the dosage form [26].

Among hydrophilic polymers, polysaccharides which are relatively complex carbohydrates are the choice material due to their non toxicity. Being natural they have certain drawbacks like purity, source and microbial contamination. If these factors can be identified and controlled, polysaccharides can be good substitute for synthetic polymer [27]. The specific application of natural polysaccharide polymers in pharmaceutical formulations include to aid in the processing of the drug delivery system during its manufacture, protect, support or enhance stability, bioavailability or patient acceptability, assist in product identification, or enhance any other attribute of the overall safety, effectiveness or delivery of the drug during storage or use [26]. Natural polysaccharides are often incorporated in the design of controlled drug delivery such as those target delivery of the drug to a specific site in the gastro intestinal tract (GIT), this can be achieved by various mechanisms including coating granules, pellets, tablets with polysaccharides having pH dependent solubility, or incorporating non-digestible polysaccharides that are degraded by bacterial enzymes present in the colon, this property makes these polysaccharides potentially useful in the formulation of colon-targeted drug delivery systems [28].

The review highlights the literatures related to the research made on plant based novel drug release-retarding materials which have been recently studied as carriers not only in the conventional sustained release dosage forms but also in chronotherapeutic drug delivery systems, gastro retentive systems, colonic drug delivery systems and microspheres. Specific reference thus is made to the use of natural polymers in the design of multiparticulate drug delivery systems as well as other new drug delivery systems under investigation.

Raju Onkar Sonawane, et al., developed extended release matrix pellets by using Lornoxicam as a model drug for prolong release of drug for an extended period of time after predetermined lag time for the chronotherapy of rheumatoid arthritis. The pellets were prepared by the Extrusion and Spheronization method using release retarding polymers like xanthan gum, xyloglucan and in combination with PVP K-30 and MCC PH-101 as pelletization aid. The effects of various formulation variables on the size and drug release were investigated. Matrix pellets containing 30% xanthan gum (XG), 30% of xyloglucan (Xg) and 30% combination of XG: Xg showed sustained release of lornoxicam for15 h [29].

Kamat Akshay Ramesh, et al., formulated an oral pulsatile drug delivery system using natural superdisintegrants and natural polymers to achieve the time release of Indomethacin, based on chronopharmaceutical approach for the treatment of rheumatoid arthritis. The press-coated pulsatile release tablet contains Indomethacin in the inner rapid release core tablet formulated by direct compression method using Plantago ovata mucilage and modified agar as superdisintegrants and the external coat was formulated using natural polymers such as dammar gum, chitosan, xanthan gum and guar gum by both direct and wet granulation method. *In-vitro* release profiles of pulsatile device during 10 h studies were found to have very good sustaining efficacy. Formulation B2 containing xanthan gum and dammar gum in the ratio of 2:1 having maximum lag time of 7h 15 min [30].

Sarojini Sarangapani,et al., prepared gastro retentive tablets of Lansoprazole. Gel-forming polymer HPMC K4M, natural polymer and gas-generating agent sodium bicarbonate were added to the drug to achieve in vitro buoyancy. The *In-vitro* release of the formulation F1and F2 (synthetic polymer) showed more drug release and F7 and F8 (natural polymer) also showed better sustained release properties than synthetic polymer. From the results of sustained release properties, it had been concluded that the novel natural polymeric material from Delonix regia may be natural and economical alternative for the formulation of floating drug delivery system. Since Delonix regia gum is of natural origin it is non-toxic, biocompatible and cheaper [31].

Dharmaraj sinh Chauhan, et al., carried out studies on colon specific matrices of Mebeverine HCl using various polysaccharides like guar gum, Locust bean gum and xanthan gum by direct compression method. Swelling studies indicated that, matrix tablets prepared with xanthan gum, XG (X4) swelled more as compared to those prepared using guar gum, GG and locust bean gum, LBG. Release profiles indicated that, increase in the polymer concentration has drastically retarded the release of Mebeverine Hcl. The optimized tablets prepared using GG (G4), LG (L4) & XG (X4) showed controlled release over periods of 24 hrs, whereas the marketed product controlled the drug release over a period of 12 hrs. The mechanism of drug release was Non-Fickian diffusion controlled first order kinetics for optimized matrix tablets of GG (G4) and LBG

(L4), whereas for XG (X4) it followed Highuchi model. The developed matrix tablets can be viewed as a better approach in the colonic delivery of Mebeverine HCl [32].

Nagamani Bolla, et al., employed microencapsulation for oral use to sustain the drug release, and to reduce or eliminate gastrointestinal irritation. Irbesartan loaded microspheres were prepared using gelatin as a base material along with kernel powder (Tamarindus indica belonging to family Fabaceae) and acacia by phase separation and Coacervation method. Kernel powder loaded microspheres has shown better control over drug release than acacia. Microspheres shown lowered bursting effect and controlled release rate. The size and compatibility of microspheres were analyzed by using SEM and FTIR respectively. This was the first report on kernel powder which is obtained from Tamarind seeds used as a control releasing agent [33].

Gandhi, et al., developed a multiparticulate system intended to utilize natural material for controlled drug delivery system. The system comprising of Cashew Gum coated pellets, designed for controlled drug delivery of Diltiazem hydrochloride. The sugar beads/pellets were loaded with drug (Diltiazem hydrochloride) using microcrystalline cellulose as a spheronizing aid and PVP K30 as a binder. Different coat weights of Cashew Gum were applied to the drug loaded pellets in Fluidized Bed Processor (FBP) to produce the controlled release drug delivery. *In-vitro* dissolution studies of the pellets performed which showed that the drug release from the coated pellets depends on the coat weights applied. Since, Diltiazem hydrochloride is a drug, which exhibits a high solubility, it would be possible to minimize drug release from coated pellets and effectively release the drug for controlled drug delivery system [34].

**Table 2: Literature review on application of Natural Polymers used in Sustained Release Tablets**

| Natural polymer | Model drug | Results | Ref |
|---|---|---|---|
| Seed powder of Strychnos potatorum | Diclofenac sodium | Seed powder when used at a concentration of 40% was capable of sustaining the release of drug up to 10 hrs. Further, purification of seed powder may improve its release retardant properties. | [17] |
| Tamarind seed polysaccharide | Metformin Hydrochloride | Tamarind gum polysaccharide being a natural polysaccharide can be administered to patients safely, thereby improving the patient compliance by releasing the drug in a sustained manner. | [22] |
| Mucilage of Aloe barbadensis miller | Glimepiride | Dried Aloe barbadensis miller mucilage and Povidone combination could be used as a matrix forming material for making Sustained release matrix tablets. | [35] |
| Resin of Artocarpus hetrophyllus (Jackfruit latex) | Theophylline | It was found that 10% of processed jack fruit latex powder was required for optimum drug release profile of sustained release tablets of theophylline. | [36] |
| Seed mucilage of Vigna mungo (Black gram) | Aceclofenac | The mucilage powder with the maximum concentration of 10 % w/w showed sustained drug release of 29.43 % at the end of 8h showing good sustained release and matrix forming capacity | [37] |
| Natural mucilage of Abelmoschus esculentus (Okra gum) | Diclofenac sodium | Sustained release matrix of the mucilage at 10-15% concentration was capable of prolonging the release of drug for 10 hrs. | [38] |
| Mucilage of Hibiscus rosasinensis Linn | Diclofenac sodium | The dried mucilage can be used as release-retarding agent for 12 h when the drug-mucilage ratio was 1:1.5. | [39] |
| Myrrh oleo gum resin (MOGR) | Domperidone | The results clearly specify the potential of MOGR could be used as binder, release retardant and mucoadhesive natural material in tablet formulations. | [40] |
| Seed mucilage of Ocimum tenuiflorum Linn | DiltiazemHCl | It was founded the seed mucilage alone does not give the desired release retardant effect but in combination with povidone shows excellent release retardant potential. | [41] |

## CONCLUSION

The market for drug delivery system has come a long way and will continue to grow at an impressive rate. Today's drug delivery technologies enable the incorporation of drug molecules into a new delivery system, thus providing numerous therapeutic and commercial advantages. Present scenario of MDDS; find a greater advantage due to its flexible design in variable release properties, stability and patient compliance. Drug release retarding polymers are the key performers in controlling the release of drug from the systems for which natural polymers play an important role. Natural materials being readily available, cost effective, eco-friendly, biodegradable and biocompatible due to their natural origin can be extensively used in the field of drug delivery. In recent years, the interest is growing to develop multiparticulate drug delivery system with the use of natural polymer thereby increasing the therapeutic value as well as reducing toxicity. The approaches in this article represent application of natural polymers as drug release retardant material with a view to design multiparticulate drug delivery systems keeping in mind the toxic effects of the drugs incorporated and to maintain the overall stability of the product on the account of the properties of natural polymers. Thus MDDS with natural polymers as drug release retardant material should be promising in the future.

## CONFLICT OF INTERESTS

Declared None

## REFERENCES

1. Kaur T, Bhawandeep G, Sandeep Kumar, Gupta GD. Mouth dissolving tablets: a novel approach to drug delivery. Int J Curr Pharm Res 2011;3(1):1-7.
2. Sirisha KVR, Vijayasri K, Devanna N, Kamalakar. Formulation and *in vitro* evaluation of Esomeprazole delayed release multi-particulate capsules. Int J Res Pharm Sci 2013;4(3):328-35.
3. Bipin Gandhi, Jagdish Baheti. Multiparticulates drug delivery systems: a review. Indian J Pharm Chem Sci 2013;2(3):1620-6.
4. NS Dey, S Majumdar, MEB Rao. Multiparticulate drug delivery systems for controlled release. Trop J Pharm Res 2008;7(3):1067-75.
5. Mahesh K Baramade, Shailesh L Patwekar. Controlled release approach to novel multiparticulate drug delivery systems. Int J Pharm Pharm Sci 2012;4(3):757-63.
6. Shaji Jessy, Shinde Amol B. Oral multiparticulate pulsatile drug delivery systems: a review. Int Res J Pharm 2011;2(2):22-7.
7. Navnit H Shah. Hoffmann La-Roche, Inc. Multi-Particulate Dosage Form for Oral Controlled Release: Development Considerations. Available from URL: *http: //mediaserver.aaps.org/meetings/09am/slides/11.8.09_sun/410 /0830/navnit_shah.pdf*
8. Khyati Patel, Upendra Patel, Bhavin Bhimani, Ghansyam Patel, Dhiren Daslaniya. Extended release oral drug delivery system. Int J Pharm Res Bio-Sci 2012;1(3):1-26.
9. Vibhav Patel, Pranav Patel, Yogeshwar Thakkar, Praful Bharadia. Multiparticulate as a potential approach for colon targeted drug delivery system: a review. Int J Univer Pharm Life Sci 2012;2(3):131-46.
10. Joana mota. Matrix-and Reservoir-type Oral Multiparticulate Drug delivery systems.[Dissertation]. Berlin; 2010. p. 2-8.
11. Kamat Akshay Ramesh, Shabaraya AR, Azharuddin Mohd. Pulsatile drug delivery systems using natural polymers as release modifiers. Int Res J Pharm 2012;3(12):42-5.

12. Kumar Amit, Ranga Sonam. Pulsatile drug delivery system: method and technology review. Int J Drug Dev Res 2012;4(4):95-107.
13. Sirisha KVR, Vijayasri K, Suresh K, Kamalakar Reddy G. Multiple unit pellet systems: a review. Int J Pharm 2012;2(2):419-25.
14. Amelia M Avachat, Rakesh R Dash, Shilpa N Shrotriya. Recent investigations of plant based natural gums, mucilages and resins in novel drug delivery systems. Ind J Pharm Edu Res 2011;45(1):86-99.
15. Krushna kumar J Gandhi, Subhash V Deshmane, Kailash R Biyani. Polymers in pharmaceutical drug delivery system: a review. Int J Pharm Sci Rev Res 2012;14(2):57-66.
16. Sandhya P, Siddiqua Habeeb, Sunitha M, Rao Patnaik KSK, Subrahmanyam CVS. A novel approach in modified release dosage forms. Formulation and evaluation of oral controlled release matrix tablets of etodolac. Asian J Pharm Res 2013;3(2):60-5.
17. Ramadevi K, Padmavathi K, Sravani N, Chandra Sekhara Rao G. Formulation and evaluation of diclofenac sodium sustained release tablets using seed powder of strychnos potatorum. Int J Biopharm 2013;4(2):110-4.
18. Nikhil Sachan K, Ghosh SK, Seema Pushkar. The Science of Polymeric plant based excipients in pharmaceutical drug delivery systems: Global perspective of Biological Researches, Seminar; 2010. p. 135-50.
19. Dharmendra S, Surendra JK, Sujata M, Shweta S. Natural excipients-a review. Int J Pharm Biol Arch 2012;3(5):1028-34.
20. Shanmugam S, Manavalan R, Venkappaya D, Sundaramoorthy, *et al*. Natural polymers and their applications. Natl Prod Radiance 2005;4(6):478-81.
21. Kumar S, Gupta SK. Natural polymers, gums and mucilages as excipients in drug delivery. Polim Med 2012;42(3-4):191–7.
22. Deveswaran R, Sravani B, Bharath S, Basavaraj BV, Madhavan V. Development of sustained release Metformin hydrochloride tablets using a Natural polysaccharide. Int J App Pharm 2012;4(2):23-9.
23. Amir Shaikh, Parvez Shaikh, Yogesh Pawar, Subhash Kumbhar, Ramesh Katedeshmukh. Effect of gums and excipients on drug release of ambroxol Hcl sustained release matrices. Int J Curr Pharm Res 2011;6(1):11-5.
24. Abu bakar, Ujjwal Nautiyal, Senthil Kumar M, Bharat Bhusan. Polymeric systems as controlled release drug products: a review. Int J Pharm Med Res 2014;2(2):72-7.
25. Gowda DV, Anjana John, Zeinul Hukuman. Preparation, Evaluation and Bioavailability studies of Propafenonr hydrochloride loaded with gum Microspheres for controlled study. Int J Pharm Bio Sci 2013;4(2):1036–49.
26. Razia Begum Sk, Mahidhar Reddy D, Jyothirmai K, Dileep Kumar GV, Jayasree S, JeevanKumar J, *et al*. A novel review on natural polymers used in formulation of pharmaceutical dosage forms. Int J Pharm Natl Med 2013;1(1):71-8.
27. Krishnarajan D, Mahesh Reddy C, Sasikanth Kanikanti, Senthil Kumar N, Purushothaman M. Formulation and evaluation of sustained release matrix tablets of levofloxacin using natural polymer. Pharmacophore 2013;4(5):146-57.
28. Kavitha Reddy, Krishna Mohan G, Shobharani Satla, Switi Gaikwad. Natural polysaccharides: versatile excipients for controlled drug delivery systems. Asian J Pharm Sci 2011;6(6):275-86.
29. Raju Onkar Sonawane, Deepali Gawale, Vishal Vijay Pandey, Pundikarao IGE. Formulation and *In-vitro* characterization of multiple unit sustained release matrix pellets of lornoxicam using natural gums. Indian J Novel Drug Delivery 2013;5(4):208-20.
30. Kamat Akshay Ramesh, *et al*. Formulation and evaluation of pulsatile drug delivery system containing indomethacin using natural polymers. Int Res J Pharm 2013;4(2):111-4.
31. Sarojini Sarangapani, Manavalan Rajappan. Lansoprazole release from a floating dosage form based on the natural polymer of delonix regia. Int J Pharm Tech Res 2012;4(3):1085-95.
32. Dharmarajsinh Chauhan, Axay Patel, Shrenik Shah. Influence of selected natural polymers on *in-vitro* release of colon targeted mebeverine HCL matrix tablet. Int J Drug Dev Res 2012;4(2):247-55.
33. Nagamani Bolla, Rajan Raju CH, Sarat Chandra K, GSN Koteswara Rao, Uma Devi P. Effect of natural polymers on controlled release of irbesartan from acacia and kernel loaded microspheres. Int J Inv Pharm Sci 2013;1(4):282-7.
34. Bipin Gandhi R, Bhatu Badgujar P, Ankit Kasliwal V. Development and *in vitro* evaluation of multiparticulate system using novel coating material for controlled drug delivery system. Int J Pharm Pharm Sci 2011;3(3):96-9.
35. Abdul Ahad, *et al*. Design and evaluation of sustained release matrix tablets of Glimepiride based on combination of natural and synthetic Polymers. Int J Appl Biol Pharm Technol 2010;1(3):770-7.
36. Vinaya OG, KG Revi kumar. Development of oral sustained release tablets of theophylline. Res J Pharm Biol Chem Sci 2012;3(4):494-506.
37. Basappa Veerabhadraiah Basavaraj, Naramsetty Saritha, Srinivasan Bharath, Rajamanickam Deveswaran, Varadharajan Madhavan. Vigna mungo mucilage-a natural polymer in the design of matrix based sr tablet of aceclofenac. Int J Pharm Sci Rev Res 2013;21(2):125-30.
38. Prakash Pawan, Kumar Nitin. Design and development of sustained release matrix tablet of diclofenac sodium using natural polymer. Int Res Pharm 2013;4(1):169-76.
39. Jani GK, Shah DP. Evaluation of mucilage of Hibiscus rosasinensis Linn as rate controlling matrix for sustained release of diclofenac. Drug Dev Ind Pharm 2008;34(8):807-16.
40. Inderbir Singh, Gurpreet Arora, Karan Malik, Sandeep Arora. Formulation and Evaluation of controlled release muchoadhesive matrix tablets: assessment of myrrh oleo gum resin as a natural pharmaceutical excipient. Int J Pharm Sci Drug Res 2011;3(2):84-8.
41. Kamble et al. Evaluation of drug release retardant potential of Ocimum tenuiflorumlinn. Seed mucilage isolated by Defatting method. Int J Pharm Chem Biol Sci 2012;3(1):68-74.