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REVIEW ON FORMULATION AND EVALUATION OF SUSTAIN RELEASE TABLET USING NATURAL POLYMER

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Abstract
The review focuses on the formulation and evaluation of sustained release tablets using natural polymers. The sustained release (SR) dosage forms are designed to release drugs over extended periods, improving therapeutic efficacy and patient compliance. The paper discusses the advantages and limitations of sustained release tablets, methods of preparation, and various natural polymers used in these formulations. Natural polymers such as chitosan, starch, cellulose, xanthan gum, guar gum, locust bean gum, and gum karaya have been highlighted for their roles in enhancing drug release profiles. The review also covers evaluation tests for sustained release tablets, including thickness, diameter, weight variation, hardness, friability, content uniformity, and in-vitro dissolution tests. The findings indicate that sustained release tablets, particularly those using natural polymers, offer significant benefits over conventional dosage forms in terms of controlled drug delivery and patient adherence.

Keywords: Sustained release tablets, natural polymers, drug delivery, chitosan, guar gum, xanthan gum, formulation methods, evaluation tests, controlled release.

Introduction
The oral route is frequently preferred for drug administration due to its versatility in dosage form design, surpassing many other routes in flexibility (Mali et al., 2015). Drug release refers to the process by which a drug becomes available for pharmacokinetic activities such as absorption, distribution, metabolism, and excretion—thereby enabling effective pharmacological action (Wilde et al., 2018). Oral drug delivery is widely used because it is more convenient compared to other administration methods and is suitable for systemic drug delivery across various pharmaceutical products and dosage forms. The popularity of the oral route stems from its distinct advantages (Souery and Bishop, 2018). For many years, polymers have been employed as excipients in conventional immediate-release oral dosage forms. These polymers, such as polyvinyl pyrrolidone and hydroxypropyl methylcellulose (HPMC), are used as binders to facilitate the preparation of granules, enhancing the flow and handling characteristics of tablet formulations. Occasionally, dosage forms may be coated with a "non-functional" polymeric film to protect the drug from degradation, mask

unpleasant tastes, or enhance the appearance of the formulation without affecting the drug release rate (Longer et al., 1985).

Sustained release, prolonged release, modified release, extended release, and depot formulations are terms used to describe drug delivery systems designed to provide or extend therapeutic effects by releasing medication continuously over an extended period after a single dose (Jantzen and Robinson, 1995). The benefits of administering a drug in a single dose that releases over an extended period, as opposed to multiple doses, have been well-recognized in the pharmaceutical industry (Altaf and Friend, 2002).

Polymer

The term "polymer" originates from two Greek words: "poly," meaning many, and "mer," meaning unit or part (Rajeswari and Bada, 2013). Polymers are large molecules, known as macromolecules, characterized by their high molecular weight. They are created by linking numerous repeating structural units, called monomers, through covalent bonds. This process of forming polymers from monomers is known as polymerization (Vinod et al., 2010). Polymers can be categorized into three main types: natural polymers, synthetic polymers, and semi-synthetic polymers.

Natural polymer

Natural polymers are those derived from natural sources, including plants and animals. They are crucial for various biological processes and applications. Notable examples of natural polymers used in pharmacy and other industries include chitosan, carrageenan, phylum, acacia, agar, gelatin, shellac, guar gum, and gum karaya. These polymers are extensively utilized in the pharmaceutical industry for functions such as emulsifying agents, adjuvants, and adhesives in packaging, and they are also valuable in the development of pharmaceutical and cosmetic products (Evans, 2009).

Advantages of Natural Polymer

1. Biocompatibility: Natural polymers are biocompatible, meaning they interact well with living systems.
2. Low environmental impact: Natural polymers come from renewable sources like plant life and animal waste, rather than oil or gas products like synthetic polymers.
3. Economic: Natural polymers are economical and readily available.
4. Part of our diet: Many natural polymers are part of our daily diet.
5. Applications in many industries: Natural polymers are used in the food, cosmetic, pharmaceutical, and prosthetic industries.
6. Water solubility: Natural polymers are water soluble.
7. Emulsifying and binding properties: Natural polymers have emulsifying and binding properties.

Chitosan: Chitosan is a polysaccharide derived from chitin through a process of deacetylation. This biopolymer is known for its non-toxic nature and cost-effectiveness. It features reactive amino groups, which make it useful across various fields. Chitosan has demonstrated applications as an antimicrobial agent in agriculture, a potential enhancer of plant defense mechanisms, an additive in the food industry, a hydrating component in cosmetics, a flocculating agent in wastewater treatment, and more recently, as a pharmaceutical agent in biomedicine (Uhrich et al., 1999). Additionally, chitosan and its derivatives, such as N-trimethyl chitosan and mono-N-carboxymethyl chitosan, have proven to be effective and safe enhancers of mucosal absorption, including nasal and oral routes (Saurabh et al., 2015).

Starch: Starch, also known as amylum, is a carbohydrate made up of numerous glucose units linked by glycosidic bonds. This polysaccharide is synthesized by green plants as a form of energy storage. It serves as the primary carbohydrate reserve in these plants, particularly in seeds and subterranean parts. Various types of starches are utilized in the pharmaceutical industry (Kulkarni et al., 2012).

Cellulose: Cellulose is a natural polysaccharide found in the cell walls of plants. It is a crucial and intriguing biopolymer that is insoluble in water and most common solvents. Cellulose has diverse applications, including use in composites, netting, upholstery, coatings, packaging, and paper products (Joshi and Patel, 2012; Benabid and Zouai, 2016).

Xanthan gum: Xanthan gum (XG) is a versatile polysaccharide valued for its wide range of applications (Kumar et al., 2024). It is produced through the fermentation of carbohydrates by the bacterium *Xanthomonas campestris*. Commonly referred to as corn sugar gum, Xanthan gum is a high-molecular-weight polysaccharide that includes D-glucose, D-mannose, and D-glucuronic acid, and contains at least 1.5% pyruvic acid. This cream-colored powder is soluble in both hot and cold water and is neutral to litmus. Xanthan gum solutions maintain optimal stability within a pH range of 4 to 10. It is widely used as a stabilizer, thickener, and emulsifier in the pharmaceutical, cosmetic, and food industries (Shanmugam et al., 2005).

Gum karaya: Karaya gum is a dried gum exudate obtained from the *Sterculia urens* tree, belonging to the Sterculiaceae family. It is also known by various names such as Sterculia gum, Karaya gum, Indian Tragacanth, or Bassora Tragacanth (Afrasim and HG, 2010; Deshmukh et al., 2009). Research has demonstrated the development of sustained-release matrix tablets for water-soluble Tramadol hydrochloride using different polymers, including Hydroxypropyl Methylcellulose (HPMC) and natural gums like Karaya gum and Carrageenan. Notably, a combination of Karaya gum and Guar gum has shown superior effectiveness in preparing sustained-release tablets compared to using the gums individually (Peter et al., 1999).

Guar gum: Guar gum is derived from the endosperm of the seeds of the legume plant *Cyamopsis tetragonolobus*. To produce guar gum, the pods are first dried in sunlight and then the seeds are manually separated. This polysaccharide consists primarily of the sugars galactose and mannose, with a backbone of mannose residues linked in a linear chain via 1,4-glycosidic bonds. Galactose residues are attached to every second mannose unit through 1,6-glycosidic bonds, creating short side branches (Mali et al., 2012). Guar gum is commonly used as a thickening agent in cosmetics and sauces, helps prevent ice crystal formation in ice creams, and is also utilized in the formulation of sustained-release tablets (Prakash et al., 2011).

Locust bean gum: Locust bean gum, also referred to as carob bean gum, is derived from the endosperm of the seeds of the carob tree (*Ceratonia siliqua*). This gum is utilized extensively in the food, cosmetic, and pharmaceutical industries as a thickening and stabilizing agent (Prakash and Kumar, 2023). In pharmaceuticals, locust bean gum is valued for its function as a controlled-release excipient in tablet formulations. Its advantages include biodegradability, low toxicity, and cost-effectiveness, which contribute to its growing use across various applications (Attwood et al., 2001).

Sustained release dosage forms

Any modification of a drug or dosage form that extends its therapeutic effect is considered a sustained release approach (Gandhi and Kumar, 2014). This method not only extends the period during which the drug is active but also ensures predictable and consistent drug release rates (Gadekar et al., 2021). Sustained release formulations aim to maintain stable blood levels of the drug, improving patient compliance and enhancing the drug's efficacy (Semwal et al., 2014). The rate at which the drug is released from these dosage forms is primarily influenced by the type and proportion of natural and synthetic polymers incorporated into the formulation (Jalwal et al., 2018).

Sustain release tablet

One straightforward method for creating sustained release dosage forms is through direct compression, where the drug, release retardant, and additional components are combined to form a tablet with the drug incorporated within a matrix of retardant material. Alternatively, the blend of drug

and retardant may be granulated before compression. These tablets are referred to as sustained release tablets. There are three main types of materials used to control the release in such tablets: insoluble or 'skeleton' matrices, water-insoluble erodible matrices, and hydrophilic matrices (Oliphant and Green, 2002). Sustained release formulations are designed to deliver an initial dose of the drug to quickly achieve the desired therapeutic effect, followed by a controlled, gradual release of the drug to sustain the effect over a set period. This approach has revolutionized drug delivery systems in pharmaceutical technology. Typically, these tablets are manufactured in micronized form to ensure that a fine particle size facilitates the rapid formation of a gelatinous layer on the tablet's surface (Chien et al., 2002).

Advantages of Sustain tablets

1. Easy to manufacture.
2. Versatile and effective
3. It has low cost.
4. Can be made to release high molecular weight compounds.
5. Suitable for both non degradable and degradable systems.
6. No danger of dose dumping in case of rupture.
7. Can be fabricated in a wide range of sizes and shapes (Vyas and Khar, 2010)

Disadvantages of Sustain tablets

1. The remaining matrix must be removed after the drug has been released.
2. The drug release rates vary with the square root of time.
3. Achievement of zero order release is difficult.
4. Not all drugs can be blended with a given polymeric matrix.
5. Water soluble drugs have a tendency to burst from the system.
6. Poor in vitro – in vivo correlation.
7. Possibility of dose dumping due to food, physiologic or formulation variables.
8. Retrieval of drug is difficult in case of toxicity, poisoning or hypersensitivity reactions (Kamboj and Gupta, 2009)

Methods of preparation

1. **Direct Compression:** In this process, powdered materials are compressed directly without changing the properties of the drug like physical and chemical (Misal *et al*., 2013).
2. **Wet Granulation:** In this method weighed quantities of drug and polymer are mixed with sufficient volume of the granulating agent. After enough cohesiveness was obtained, the mass is sieved through 22/44 mesh. The granules are dried at 40°C and after that kept in a desiccator at room temperature. Once the granules dried are retained on 44 meshes were mixed with 15% of fines. Lubricants and Glidants are added and the tablets are compressed using a tablet compression machine (Lachman *et al*., 1989).
3. **Melt Granulation:** This substance can be added in the molten form over the substrate, which is then heated above its melting point. In melt granulation, meltable substance act as liquid binding agent and hence does not require the use of organic solvents. Various lipophilic binders such as Glyceryl Palmitostearate were used in melt granulation technique (Misal *et al*., 2013).
4. **Hot-Melt Extrusion Process:** In the hot-melt extrusion process, a mixture of the active ingredients, the thermoplastic polymers and other processing aids is fed into the barrel of the extruder through the hopper. The materials are transferred inside the heated barrel by a rotating screw (Shah *et al*., 2015).

Evaluation Test for sustained release tablets

Thickness and Diameter: Micrometer screw gauge is used for determining thickness and diameter of tablets (Zalte and Sauddagar, 2013).

Weight Variation: Average weight of twenty tablets is calculated and compared with weight of one tablet. It is an important aspect for quality control as all tablets must be of uniform weight in one batch. The U.S Pharmacopoeia allows a little variation in the weight of a tablet (Venkateswarlu and ShanthI, 2012). The following percentage deviation in weight variation is allowed

Table No 1: Percentage deviation in weight variation

Average weight of a tablet	Percentage deviation
200mg or less	10
More than 190 mg and less than 200 mg	7.5
200 or more	5

Hardness test: Monsanto hardness tester is used to determine hardness of tablets. It is expressed in Kg/cm^2 (Singh *et al*., 2018)

Friability test: friabilator is used to determine friability of tablets at 25rpm for 4 min (Andrew *et al*., 2023). The percentage friability was then calculated by,

$$F = \frac{W_{initial} - W_{initial}}{W_{initial}} \times 100$$

% Friability of tablets less than 1% is considered acceptable.

Content uniformity: The uniformity of drug content is determined by dissolving tablet in a suitable solvent of pH 7.4 phosphate buffer and analyzing sample in UV spectrophotometer (Ali and Alsaifi, 2018).

In-vitro dissolution test: Rotating Paddle apparatus is generally used to determine drug release. The amount of drug released in dissolution media is determined using UV spectrophotometer at specific time periods. A graph of percent release of drug versus time is plotted (Shraddha *et al*., 2019).

Table 2: Different drugs, polymers and technique used in sustained release tablets

S. No.	Drug	Polymer	Technique	References
1	Ketorolac tromethamine	Tamarind Gum, Tapioca Starch and Chitosan	Direct compression	Buddhadev *et al*., 2024
2	Venlafaxine	Guar gum	Direct compression method	Yadav *et al*., 2024
3	Atorvastatin	(guar gum, xanthan gum, hibiscus gum, okra gum, and soya bean gum	Direct compression method	Manyam *et al*., 2023
4	Propranolol Hydrochloride	Gum Acacia, Hibiscus Rosasinesis and Microcrystalline cellulose.	Direct compression	Purohit *et al*., 2022
5	Lansoprazole	Xanthan gum, Gellan gum and Chitosan	Direct compression	Jain and Banveer, 2021
6	Glibenclamide	Locust bean gum and Karaya gum	Direct compression method	Ramteke *et al*., 2019

Conclusion

This review article has been focused on the sustained release tablets, advantages and disadvantages and the various polymers used to formulate such system. Natural polymers play a vital role in the preparation of pharmaceutical formulation. It is used as pharmaceutical excipients. The conclusion of the above discussion is that the sustain tablets are useful in overcoming patient compliance issues and

dosage form efficiency issues that are related to conventional dosage forms' inability to produce the required therapeutic response. Along with other advantages, cost-efficient and a single or every day intake are the pluses. As a result, the dosage form design is being optimised for sustained release tablets.

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