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Review Article

Sustain Released Tablet by Using Natural Gum

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ABSTRACT

New natural excipients are being found, and old excipients are finding new uses, due to the quest for plentiful natural gums and the goal to reduce the amount of artificial excipient utilized in the creation of formulations. They are being utilized in formulation development more frequently because they are secure and efficient. It is not what is expected that natural gums and polymers would be used in the creation of pharmaceutical formulations because of batch-to-batch fluctuation and inconsistent content consistency. The process of applying Furthermore, natural gum is less expensive than many of the excipients now in use. Mucilage and gums are examples of natural materials in both traditional and cutting-edge medication delivery techniques. To determine how natural polymers can be used to control the discharge of medications from formulations in various dosage forms and to show how useful they are in pharmaceutical drug carrier systems. Their main purpose is to distribute drugs in a regulated or sustained manner. Tests were conducted on the physical and chemical characteristics. This article contains information regarding the use of natural gums.

INTRODUCTION

Pharmaceutical formulations called sustained release tablets, sometimes referred to as extended-release or controlled-release tablets, are made to release their active components gradually over a longer period of time. Maintaining therapeutic concentrations in the body for a prolonged duration. In the realm of modern pharmacotherapy, the creation of innovative medication delivery methods has revolutionized the way medications are administered, providing innovative solutions to optimize therapeutic outcomes while minimizing adverse effects. Among these advancements, sustained release tablets have emerged as a cornerstone in pharmaceutical formulations, offering a paradigm shift from conventional immediate-release formulations to controlled and prolonged drug delivery strategies [1].

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Unlike their immediate-release counterparts, which deliver the entire dose of medication rapidly upon ingestion, sustained release tablets are designed to release their contents steadily and continuously, maintaining therapeutic concentrations of the drug in the body over an extended duration [2].

The development of sustained release tablets stems from the recognition of the limitations inherent in conventional dosage forms, particularly with respect to dosing frequency, fluctuations in drug plasma levels, and patient compliance. Traditional immediate-release formulations often require frequent dosing intervals, leading to challenges in patient adherence and therapeutic efficacy, especially in the management of chronic conditions requiring long-term medication regimens [3,4].

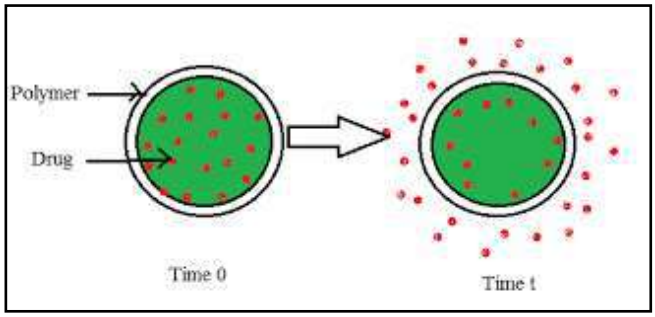

Fig. 1: Sustained Release Tablets

By contrast, sustained release tablets offer several key advantages that address these limitations and enhance the pharmacokinetic and pharmacodynamic profiles of medications. One of the primary benefits of sustained release formulations is their ability to reduce dosing frequency, allowing for simplified medication regimens and improved patient compliance. By distributing the medication gradually over a long time, sustained release tablets minimize the need for frequent administrations while ensuring continuous therapeutic drug levels in the body [5-7].

Moreover, sustained release tablets can provide a more consistent and controlled drug release profile, leading to smoother drug plasma concentration-time curves and reduced fluctuations in drug levels. This controlled release mechanism not only optimizes the therapeutic efficacy of medications but also minimizes the risk of side effects associated with peak drug concentrations, particularly for drugs with narrow therapeutic indices or dose-dependent adverse effects [8,9].

The development of sustained release tablets encompasses a diverse array of formulation strategies, excipients, and technologies aimed at achieving the intended therapeutic effects and release kinetics [10]. From matrix-based systems to osmotic pumps and multi particulate formulations, sustained release technology offers versatility and flexibility in tailoring drug delivery profiles to meet the specific requirements of different drugs and patient populations [11].

In light of these advancements, sustained release tablets have found widespread applications across various therapeutic areas, ranging from chronic diseases requiring long-term therapy to acute conditions necessitating prolonged drug action. Whether it's improving the management of hypertension, diabetes, pain, or psychiatric disorders, sustained release formulations have become indispensable tools in the modern pharmacotherapeutic armamentarium [12].

This review seeks to offer a thorough summary of sustained release tablets, exploring their mechanisms of action, formulation strategies, pharmaceutical applications, and future perspectives. By delving into the intricacies of sustained release technology, we seek to elucidate the significance of these dosage forms in modern drug delivery and their role in advancing patient care and therapeutic outcomes in clinical practice.

Unlike immediate-release tablets, which rapidly release their contents upon ingestion, sustained release tablets offer several important advantages in pharmaceutical formulations [13-16]:

Improved Patient Compliance: Sustained release tablets typically require less frequent dosing compared to immediate-release formulations. This reduced dosing frequency can lead to improved patient compliance by simplifying medication regimens and reducing the likelihood of missed doses.

Enhanced Therapeutic Efficacy: By delivering medication steadily over an extended period, sustained release tablets can help maintain therapeutic concentrations of the active ingredient within the therapeutic window for a longer duration. This sustained exposure to the drug can lead to improved efficacy in managing chronic conditions and better control of symptoms.

Minimized Side Effects: The controlled release of active ingredients provided by sustained release tablets can help minimize fluctuations in drug plasma levels, reducing the incidence of side effects associated with peak drug concentrations. This can be particularly beneficial for drugs with a narrow therapeutic index or those known to cause dose-dependent side effects.

Reduction of Administration Frequency: For medications requiring frequent dosing, sustained release formulations offer the advantage of reducing the number of daily administrations. This can be particularly advantageous for medications with brief half-lives or those that need to be taken multiple times a day to maintain therapeutic effects.

Enhanced Pharmacokinetic Profiles: Sustained release tablets can modify the pharmacokinetic profile of drugs, prolonging their absorption, distribution, and elimination processes. This can result in smoother drug plasma concentration-time curves, reduced fluctuations in drug levels, and potentially improved bioavailability.

Tailored Drug Delivery: Sustained release formulations allow for customized drug delivery profiles tailored to the specific therapeutic requirements of different medications and patient populations. This flexibility in drug release kinetics enables optimization of treatment regimens and better adaptation to individual patient needs.

Overall, sustained release tablets play a crucial role in pharmaceutical formulations by offering improved patient convenience, enhanced therapeutic outcomes, and minimized side effects compared to conventional immediate-release formulations. Their importance in the treatment of various medical conditions, ranging from chronic diseases to acute conditions requiring long-term therapy, underscores the significance of sustained release technology in modern pharmacotherapy [17].

Mechanisms of Sustain Released Tablet:

The mechanisms underlying sustained release tablets are diverse and can vary depending on the formulation strategy, excipients used and specific requirements of the drug being delivered. However, several common mechanisms contribute to the controlled and prolonged release of active pharmaceutical ingredients (APIs) from sustained release tablets [18-21]:

Matrix Dispersion:

Matrix dispersion is a fundamental mechanism employed in sustained release tablets where the API is uniformly distributed within a matrix of hydrophilic or hydrophobic excipients.

In hydrophilic matrices, such as cellulose derivatives (e.g., hydroxypropyl methylcellulose, HPMC), the tablet matrix swells upon contact with gastrointestinal fluids, forming a gel layer around the API. This gel layer controls the diffusion of the drug molecules out of the tablet, resulting in sustained release.

Hydrophobic matrices, such as waxes or lipids, retard drug release by controlling the penetration of water into the tablet, thereby slowing down drug dissolution and release.

Osmotic Pressure:

Osmotic pressure-based systems, often referred to as osmotic pumps, utilize osmotically active agents (e.g., salts) to generate osmotic pressure within the tablet core.

When exposed to water in the gastrointestinal tract, the tablet core swells, causing the release of the drug through an orifice or permeable membrane at a controlled rate. The osmotic gradient drives water influx into the tablet core, pushing the drug solution outwards.

Ion-Exchange Resins:

Ion-exchange resins can be incorporated into sustained release tablets to control drug release through ion exchange mechanisms.

Positively charged drug molecules are bound to the negatively charged resin matrix, and drug release occurs as ions from the surrounding environment displace the drug molecules from the resin, thus regulating the release rate.

Coating Systems:

Coating systems, such as film coatings or enteric coatings, can be applied to tablets to modulate drug release kinetics.

Film coatings may provide a barrier that controls the rate of drug diffusion or dissolution from the tablet core, while enteric coatings protect the drug from acidic conditions in the stomach and ensure release in the alkaline environment of the intestine.

Multiparticulate Systems:

Multiparticulate sustained release formulations consist of multiple small particles or pellets containing the drug. These particles may be coated with polymers or encapsulated within microspheres to achieve sustained release by controlling drug diffusion or erosion.

Swelling and Erosion:

Some sustained release tablets rely on swelling and erosion mechanisms to control drug release. Swelling polymers, such as sodium carboxymethylcellulose (NaCMC) or polyethylene oxide (PEO), imbibe water upon exposure to gastrointestinal fluids, leading to tablet expansion and controlled drug release. Erosion of the tablet matrix further contributes to drug liberation.

These mechanisms can be employed individually or in combination to achieve the desired release kinetics for a given drug and formulation. By leveraging these diverse mechanisms, sustained release tablets offer precise control over drug release rates, enabling prolonged therapeutic effects and improved patient outcomes.

Preparation techniques: [22–25]

Direct Compression:

In this method, powdered materials are compressed straight without affecting the drug's chemical or physical characteristics.

Wet Granulation:

This process involves mixing an adequate amount of granulating agent with weighed amounts of the medication and polymer. Screening of wet bulk came next, once sufficient cohesion was achieved. Using a single-punch tablet compression machine, the dried and screened granules are combined with lubricant and disintegrants to create "running powder" tablets.

Melt Granulation:

This technique uses a material that melts at a comparatively low temperature. When the substrate is heated above its melting point, this material can be poured on top of it in a molten state. We experimented with various lipophilic binders utilizing the melt granulation process.

Hot Melt Extrusion Process:

The hot-melt extrusion technique involves feeding a mixture of thermoplastic polymers, active chemicals, and other processing aids through the hopper into the extruder's barrel. A revolving screw moves the materials inside the heated barrel. At high temperatures, the materials melt, and the molten mass is continually fed through the die that is fastened to the barrel's end. Films can also be made from the extruder, depending on the size of the die cylinders.

Assessment of Sustained release Tablets: [26,27]

A product's strength, safety, stability, and dependability must be ensured before a sustained release product is marketed by developing an in-vitro and in vivo analysis and a correlation between the two. The evaluation criteria and processes for formulations with sustained release have been covered by a number of writers.

Weight Variation: Twenty tablets were weighed individually and then collectively; average weight of the tablets was calculated.

Hardness: Hardness test was conducted for tablets from each batch using Monsanto hardness tester and average values were calculated.

Friability: The tablets were tested for friability testing using Roche friabilator, which revolves at 25rpm for 4min.

Thickness: The thicknesses of tablets were determined using micrometer screw gauge.

Content Uniformity: Using UV Visible spectrophotometer found the amount of the drug using the calibration curve method.

KINETIC STUDIES:

***In-Vitro* Dissolution Study:**

The Rotating Paddles equipment is typically used to determine drug release studies. Buffer is mostly employed as a dissolving medium. The bath's temperature is kept at 37 ^{0}C, and a needed sample of the drug-releasing dissolving medium is removed on a regular basis and replaced with an equal amount of the medium. To measure the amount of medication released, a UV spectrophotometer is used. The drug that dissolves at a given time is plotted as a percentage release against time.

STABILITY STUDIES:

Short Term Stability Study:

To determine change in vitro release profile on storage, a short-term stability study of the optimal batch.

In–Vivo Methods:

Once the satisfactory in-vitro profile is achieved, it becomes necessary to conduct in-vivo evaluation and establish in-vitro in-vivo correlation.

The various in-vivo evaluation methods are

- Clinical response
- Blood level data
- Urinary excretion studies
- Nutritional studies
- Toxicity studies
- Radioactive tracer techniques

Influence of formulation parameters:

Polymer concentration: The concentration of polymer in the tablet formulation plays a crucial role in controlling drug release. Typically, higher polymer concentrations result in slower drug release due to increased matrix density, which hinders the diffusion of the drug molecules out of the tablet. Conversely, lower polymer concentrations may lead to faster release kinetics [28].

Drug-to-polymer ratio: The ratio of drug to polymer in the formulation can significantly influence the release profile. A higher drug-to-polymer ratio tends to result in faster release rates as there is less polymer available to control drug diffusion. Conversely, a lower drug-to-polymer ratio may lead to slower release kinetics due to the increased polymer matrix [28,29].

Polymer type: Different types of polymers exhibit varying swelling and erosion properties, which directly impact drug release kinetics. Hydrophilic polymers, such as hydroxypropyl methylcellulose (HPMC) and sodium carboxymethylcellulose (NaCMC), typically form gel layers upon hydration, leading to controlled release by diffusion. In contrast, hydrophobic polymers like ethylcellulose and polyvinyl acetate are more suitable for providing sustained release through erosion of the polymer matrix [29].

Particle size and morphology: The particle size and morphology of both the drug and polymer can influence the surface area available for drug

release and affect the overall release kinetics. Smaller particle sizes generally result in faster release rates due to increased surface area for diffusion, while larger particles may provide sustained release by forming a denser matrix [29].

Compression force: The compression force applied during tablet manufacturing can affect the porosity and density of the tablet matrix, thereby influencing drug release kinetics. Higher compression forces often lead to denser tablets with slower release rates due to reduced porosity and hindered drug diffusion [29,30].

Excipients: Various excipients, such as fillers, disintegrants, and lubricants, can also impact drug release kinetics by affecting tablet hardness, disintegration, and erosion properties. For example, the inclusion of hydrophilic excipients like lactose may enhance water uptake and promote faster drug release [30].

Gums' Chemical Properties:

Gums are polysaccharides that hydrolyze to become monosaccharides. Hexose (such as starch and cellulose) and pentosan (such as xylan) are examples of the different hydrolysis products. The potassium, calcium, and magnesium compounds known as "polyuronides" are found in gums. Galactose and arabinose are the sugars found in gums. By hydrolyzing a polysaccharide, sugar-forming units can be identified using a variety of chromatographic methods. The phenol-sulfuric acid method can be used to assess the total number of carbohydrates in a polysaccharide as well as the number of monosaccharides present. Gum structure identification also makes use of mass spectrometry and NMR methods [31].

Grouping of Gums:

Large amounts of gums are present in a wide range of land-plant sources, including gum tragacanth, gum arabica, gum ghatti, and karaya gum; animal sources, including chondroitin sulfate, hyaluronic acid, chitin and chitosan, and seaweeds; brown algae sources, including alginate and laminarin; and fungi and other microbial sources, including xanthan, dextran, curdian, pullulan, zanflo, emulsan, schizophyllan, lentinan, krestin, scleroglucan, and Baker's yeast glycan. Among them, plant sources account for the largest amounts (Fig. 2) [32, 33].

Gums Made from Plants and Their Use in Medicine:

Polysaccharides generated from various plant sections are known as plant-derived gums (Table 1). One of the most popular gums is gum tragacanth, which has been used medicinally for a long time. Theophrastus, in the third century B.C., outlined its uses in writing.

Table 1: Plant-Based Gums

Substances	Botanical Name	Family	Structure	Pharmaceutical Applications	Ref.
Guar gum	Cyamopsis tetragonoloba	Fabaceae	Galactose Mannose	Sustained release drug delivery Suspending agent	[34–37]
Almond Gum	Prunus dulcis	Rosaceae	Aldobionic acid L-arabinose L-galactose D-mannose	Emulsifying Thickening Suspending Adhesive Stabilizing ↑Drug release Uncoated tablet dosage form	[38]

Karaya gum	Firmiana implex	Malvaceae	α-d-galacturonic acid α-l-rhamnose	↑Dissolution rate of drug solid dispersions Suspending agent Emulsifying agent Dental adhesive Sustaining agent Mucoadhesive Buccoadhesive	[39]
Tragacanth gum	Astragalus brachycalyx	Fabaceae	Pectinaceous Arabino galactans Xylogalacturonans	Sustain release Suspending agent Emulsifying agent	[40–42]
Tamarind gum	Tamarindus indica	Fabaceae	Glucosyl: Xylosyl: Galactosyl 3:2:1	Matrix tablets ↓Drug release Biodegradable carrier for colon specific release	[23]
Grewia gum	Grewia mollis	Malvaceae	Glucose Rhamnose Galacturonic acid	Controlled release dosage forms Suspending agent Binding property ↑Degree of packing ↑Fluidity of granules Film forming property	[43–48]
Gum acacia	Acacia nilotica	Fabaceae	1,3-linked β-dgalactopyranosyl	Binder Suspending agent Emulsifying agent Demulcent Emollient	[49,50]
Khaya gum	Khaya grandifoliola	Meliaceae	Protein Sugar Phenol 61% Galactose 14% Arabinose 7% Rhamnose, 8% Glucose 5% Glucuronic acid	Binding agent Drug targeting Controlled release	[51,52]
Locust bean gum	Ceratonia siliqua	Fabaceae	D-galactoDmannoglycan pentane Proteins Cellulose	Super disintegrant Controlled drug delivery Drug targeting to the colon Super disintegrants Mucoadhesive	[53–56]
Terminalia catappa gum	Terminalia catappa	Combretaceae	-	Oral sustained release tablets	[57]
Okra gum	Abelmoschus esculentus	Malvaceae	Galactose Galacturonic acid Rhamnose Glucose Mmannose Arabinose Xylose	Controlled release tablet Sustained-release tablets Suspending agent	[58]
Gum ghatti	Anogeissus latifolia	Combretaceae	β-1-3-linked D galactose units with some ß1-6- linked D-galactose units	Binder Emulsifier Suspending agent	[59,60]
Albizia gum	Albizia zygia	Fabaceae	Galactose Mannose Arabinose Glucuronic	Tablet binder Emulsifier	[61,62]

			acid 4-0-α-methyl analogue		
Cashew gum	Anacardium occidentale	Anacardiaceae	Galactose Arabinose Rhamnose Glucose Glucuronic acid L-arabinose L-rhamnose D-galactose Glucuronic acid	Suspending agent ↑Disintegration time ↓Drug release to a greater extent	[63–65]
Bhara gum	Terminalia bellirica	Combretaceae	ß-sitosterol Gallic acid Ellagic acid Ethyl gallate Galloyl glucose Chebulaginic acid	Sustained release Microcapsules employing bhara gum ↓release of famotidine	[66,67]
Cordia gum L.	Cordia myxa	Boraginaceae	Galactose (27%) Rhamnose (21%) Mannose (17%) Xylose (11%) Glucose (10%) Arabinose (9.5%) and uronic acids (5%)	Oral sustained release matrix tablets	[62]
Honey Locust Gum	Gleditsia triacanthos	Fabaceae	Proteins Fats Carbohydrates Fibers	Matrix tablets at different concentrations (5% and 10%)	[64,68]
Tara Gum	Caesalpinia spinosa	Fabaceae	Galactomannans	Controlled release carrier	[69,70]
Neem Gum	Azadirachta indica	Meliaceae	Mannose Glucosamine Arabinose Galactose Fucose Xylose	Binding property Sustained release ↑Matrix tablet	[71,72]
Moringa oleifera Gum	Moringa oleifera	Moringaceae	Arabinose Galactose Glucuronic acid Rhamnose	Gelling property Binding property Release retardant property Disintegrating property Emulsifying property	[73–76]
Gum Damar	Shorea javanica	Dipterocarpaceae	40% Alpha resin 22% Beta-resin 23% Dammarol acid 2.5% Water	Sustained release	[77,78]
Hakea Gum	Hakea gibbosa	Proteaceae	Glucuronic acid Galactose Arabinose Mannose Xylose	Sustained release Binding agent	[79–81]
Mango Gum	Mangifera indica	Anacardiaceae	----------	Binding agent Sustained release Disintegrating	[82,83]
Olibanum Gum	Boswellia serrata	Burseraceae	5–9% Oil content 13–17% Resin acids, 20–30% Polysaccharides 40–60% boswellic acid	Sustained release Binding agent	[84,85]
Terminalia Gum Baker	Terminalia randii	Combretaceae	----------	Binding agent ↑Strength friability ↓Friability	[86]
Konjac Glucomannan	Amorphophallus konjac	Araceae	D-glucose D-mannose	Gelling properties	[87]

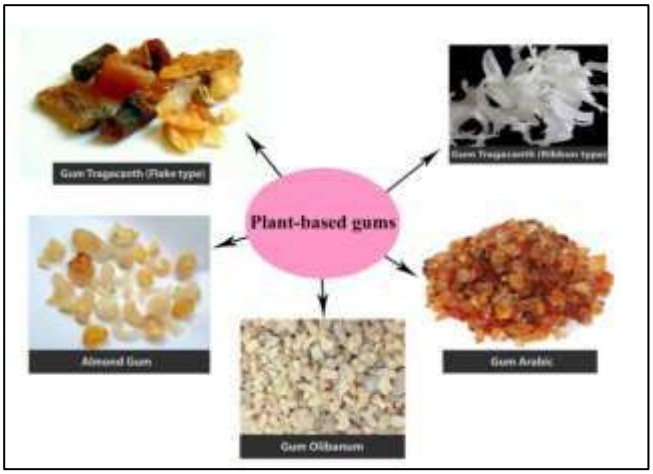

Fig. 2: Several of the most significant gums ever used

FUTURE PERSPECTIVES

The review offers a forward-looking perspective on the future of sustain released tablets using natural gums. It envisages advancements in formulation design, such as the development of multifunctional tablets capable of targeted drug delivery and on-demand release. Additionally, it explores the potential of natural gums in enabling innovative drug delivery routes and addressing emerging healthcare challenges, such as chronic diseases and personalized medicine.

CONCLUSION:

In conclusion, sustain released tablets formulated with natural gums hold tremendous potential for revolutionizing drug delivery systems. By capitalizing on the inherent advantages of natural gums and embracing technological advancements, future formulations can offer enhanced therapeutic efficacy, improved patient outcomes, and sustainability in pharmaceutical manufacturing. This review provides a comprehensive roadmap for researchers, clinicians, and industry stakeholders to navigate the evolving landscape of sustain release tablet formulations using natural gums.

Oral drug delivery is the recommended mode of administration. This aids in sustaining drug consumption and can lessen the unpredictability brought on by several dosages given during the day. Due to its sustained release nature, Sustained Release Dosage Form enhances patient compliance. Natural polysaccharides have a major role in the formulation and development of novel controlled release dosage forms utilized by human health care systems. The utilization of natural polysaccharides in the creation of controlled release dosage forms has increased dramatically in recent years. Gum was used into medicinal formulations as a release retardant. Additionally, the gum's ability to retard declines with a decrease in polymer concentration. The gum's ability to retard medication release grows as the concentration of polymer does, ensuring that the drug release is adequately regulated. This study indicates that gum has a great deal of potential to replace traditional release retardants.

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