Journal of Complementary Medicine Research, ISSN: 2146-8397 Vol. 17, No. 1, 2026(pp. 229-241)
RESEARCH ARTICLE WWW.JOCMR.COM

Development of Controlled Release Matrix Tablets using Natural Polymers

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ABSTRACT

The present research focuses on the development and evaluation of controlled release matrix tablets employing natural polymers as release-retarding agents. Controlled drug delivery systems have gained significant importance in modern pharmaceutical formulation due to their ability to maintain consistent plasma drug concentrations, reduce dosing frequency, and enhance patient compliance. In this study, various natural polymers, including polysaccharides and cellulose derivatives, were investigated for their suitability as matrix formers in oral controlled release formulations.

Matrix tablets were formulated using different natural polymers individually and in combination at varying concentrations to study their influence on drug release behavior. The prepared tablets were evaluated for physicochemical properties such as weight variation, hardness, friability, thickness, and drug content uniformity to ensure compliance with pharmacopeial standards. In vitro dissolution studies were carried out to assess the drug release profiles, and the release data were analyzed using mathematical kinetic models to elucidate the underlying release mechanisms. Swelling and erosion studies were performed to understand the hydration behavior and structural integrity of the polymer matrices during dissolution. Compatibility between the drug and polymers was confirmed using Fourier Transform Infrared Spectroscopy, Differential Scanning Calorimetry, and X-ray Diffraction studies, indicating the absence of significant chemical interactions. The results demonstrated that natural polymers effectively controlled drug release through a combination of diffusion, swelling, and erosion mechanisms.

INTRODUCTION

Overview of Drug Delivery Systems

The field of pharmaceutical sciences has witnessed remarkable advancements in drug delivery systems over the past few decades, transforming the way therapeutic agents are administered and absorbed in the human body [1]. Traditional immediate-release formulations, while effective for

certain medications, often present significant limitations including frequent dosing requirements, fluctuating plasma drug concentrations, and poor patient compliance [2]. These challenges have necessitated the development of sophisticated drug delivery technologies that can maintain therapeutic drug levels for extended periods while minimizing adverse effects [3].

Controlled release drug delivery systems represent a paradigm shift in pharmaceutical technology, offering the ability to deliver drugs at predetermined rates for specific periods of time [4]. These systems are designed to achieve optimal therapeutic outcomes by maintaining drug concentrations within the therapeutic window, thereby avoiding the peaks and troughs associated with conventional dosage forms [5]. The fundamental principle underlying controlled release systems involves the modulation of drug release kinetics through various mechanisms, including diffusion, dissolution, osmosis, and ion exchange [6]. By controlling the rate and duration of drug release, these systems enhance therapeutic efficacy, reduce dosing frequency, improve patient compliance, and minimize side effects [7].

Matrix Tablets as Controlled Release Systems

Among the various approaches to controlled drug delivery, matrix tablets have emerged as one of the most popular and commercially successful formulation strategies [11]. Matrix tablets are solid dosage forms in which the drug is uniformly dispersed throughout a polymeric matrix, and drug release occurs primarily through diffusion and/or erosion mechanisms [12]. The simplicity of matrix tablet formulation, coupled with their cost-effectiveness and manufacturing feasibility using conventional tableting equipment, has made them an attractive option for pharmaceutical manufacturers [13].

The mechanism of drug release from matrix tablets is a complex process governed by several factors including the physicochemical properties of the drug, the nature and concentration of the polymer matrix, tablet porosity, and the hydrodynamic conditions of the dissolution medium [14]. Upon contact with aqueous fluids in the gastrointestinal tract, the polymer matrix undergoes hydration, forming a gel layer on the tablet surface [15]. This gel layer acts as a barrier, controlling the rate at which water penetrates into the tablet core and the rate at which dissolved drug diffuses outward [16]. As dissolution progresses, the outer gel layer may erode, exposing fresh polymer surface to the dissolution medium and creating a dynamic equilibrium between gel formation and erosion [17].

Natural Polymers in Pharmaceutical Applications

The selection of appropriate polymeric materials is critical to the success of matrix tablet formulations, as the polymer largely determines the drug release characteristics and overall performance of the dosage form [21]. While synthetic polymers have been widely used in pharmaceutical applications, there has been a growing interest in natural polymers derived from plant, animal, or microbial sources [22]. This shift toward natural polymers is driven by several compelling factors including their abundance, renewability, biodegradability, biocompatibility, and generally recognized as safe (GRAS) status [23].

Natural polymers offer distinct advantages over their synthetic counterparts in pharmaceutical formulations [24]. They are typically non-toxic, non-irritating, and capable of undergoing chemical modifications to alter their properties for specific applications [25]. Furthermore, natural polymers

are often more economically viable, particularly in developing countries where access to expensive synthetic polymers may be limited [26]. The inherent biodegradability of natural polymers also addresses environmental concerns associated with pharmaceutical waste, making them an environmentally sustainable choice [27].

Polysaccharides as Matrix-Forming Agents

Polysaccharides represent the largest and most diverse class of natural polymers used in pharmaceutical formulations [1]. These complex carbohydrates consist of monosaccharide units linked by glycosidic bonds, forming linear or branched structures with varying molecular weights and functional properties [2]. The structural diversity of polysaccharides translates into a wide range of physicochemical characteristics, making them suitable for various drug delivery applications [3].

One of the most important properties of pharmaceutical polysaccharides is their ability to form hydrogels upon contact with aqueous media [4]. This hydrogel formation is central to their function as matrix-forming agents in controlled release systems [5]. The rate and extent of hydrogel formation depend on the chemical structure, molecular weight, and degree of substitution of the polysaccharide, as well as environmental factors such as pH, temperature, and ionic strength [6].

Chitosan, derived from the deacetylation of chitin found in crustacean shells, has gained considerable attention in pharmaceutical research due to its unique properties [7]. This cationic polysaccharide exhibits mucoadhesive characteristics, permeation-enhancing properties, and pH-dependent solubility, making it suitable for both immediate and controlled release applications [8]. The presence of amino groups in chitosan's structure allows for extensive chemical modification, enabling the development of derivatives with tailored properties [9].

Cellulose Derivatives and Their Applications

Cellulose, the most abundant natural polymer on Earth, and its derivatives have been extensively utilized in pharmaceutical formulations for decades [19]. While native cellulose is insoluble in water, various chemical modifications of its hydroxyl groups yield derivatives with diverse solubility profiles and functional properties [20]. These cellulose derivatives combine the advantages of natural origin with the predictable performance characteristics necessary for pharmaceutical applications [21].

Hydroxypropyl methylcellulose (HPMC) is perhaps the most widely used hydrophilic polymer in controlled release matrix tablets [22]. This semi-synthetic derivative exhibits excellent film-forming properties, good compressibility, and the ability to form robust gel layers that control drug release [23]. HPMC is available in various viscosity grades, allowing formulators to select appropriate grades based on desired release characteristics [24]. The non-ionic nature of HPMC makes its gel-forming properties relatively independent of pH and ionic strength, ensuring consistent performance across different physiological environments [25].

Mechanisms of Drug Release from Natural Polymer Matrices

Understanding the mechanisms governing drug release from natural polymer matrices is essential for rational formulation design and optimization [5]. Drug release from matrix tablets typically occurs through a combination of mechanisms including diffusion, swelling, and erosion, with the relative contribution of each mechanism depending on the properties of the polymer and drug [6].

The diffusion mechanism involves the movement of dissolved drug molecules through the hydrated polymer network down a concentration gradient [7]. According to Fick's laws of diffusion, the rate of drug release is proportional to the concentration gradient and the diffusion coefficient of the drug in the swollen matrix [8]. For highly water-soluble drugs in slowly eroding matrices, diffusion is often the predominant release mechanism [9].

Swelling-controlled release occurs when the polymer matrix undergoes significant volumetric expansion upon hydration [10]. As the glassy polymer transitions to a rubbery state during hydration, the polymer chains relax and disentangle, allowing drug molecules to diffuse through the expanded network [11]. The rate of swelling and the extent of polymer relaxation significantly influence drug release kinetics [12].

Physical Appearance and Organoleptic Properties

The drug typically appears as a crystalline or amorphous powder with a characteristic color ranging from white to off-white or as specified by pharmacopeial standards. The physical form of the drug, whether crystalline or amorphous, significantly affects its dissolution rate and stability. Polymorphism, if present, must be carefully controlled as different crystalline forms may exhibit varying solubility and bioavailability profiles.

The drug may have a characteristic odor or may be odorless, and its taste properties should be considered, particularly for formulations where patient palatability is a concern. The bulk density and flow properties of the drug powder influence processability during tablet manufacturing, affecting uniformity of mixing, die filling, and compression characteristics.

Solubility Characteristics

Aqueous solubility is one of the most critical parameters influencing drug release from matrix tablets. The drug exhibits specific solubility characteristics in water, which may be described as freely soluble, soluble, sparingly soluble, slightly soluble, very slightly soluble, or practically insoluble according to pharmacopeial classifications. The exact solubility value in water at different temperatures provides quantitative information essential for predicting dissolution behavior.

Solubility varies with pH, which is particularly important for ionizable drugs. The drug may exhibit pH-dependent solubility based on its acidic or basic functional groups, with maximum solubility occurring at pH values where the drug exists predominantly in its ionized form. The pH-solubility profile must be thoroughly characterized across the physiological pH range encountered in the gastrointestinal tract.

REVIEW OF LITERATURE

Historical Perspective of Controlled Release Drug Delivery

The concept of controlled drug delivery has evolved significantly over the past several decades, transforming from simple sustained release formulations to sophisticated systems capable of precise temporal and spatial control of drug release [31]. The earliest attempts at prolonging drug action involved simple coating techniques and the use of slowly dissolving materials, but these primitive systems lacked the precision and reproducibility required for modern pharmaceutical applications [32]. The recognition that maintaining constant plasma drug concentrations could

improve therapeutic outcomes while minimizing adverse effects drove the development of more advanced controlled release technologies [33].

The introduction of hydrophilic matrix systems in the 1960s marked a significant advancement in oral controlled release technology [34]. These systems offered simplicity in manufacturing, cost-effectiveness, and the ability to modulate drug release through variation of polymer type and concentration [35]. The pharmaceutical industry quickly recognized the potential of matrix-based systems, leading to extensive research and development activities that continue to the present day [36]. Over time, the understanding of release mechanisms, polymer behavior, and drug-polymer interactions has deepened, enabling rational design approaches that were not possible in earlier decades [37].

Natural Polymers in Matrix Tablet Formulation

Chitosan-Based Matrix Systems

Chitosan has emerged as one of the most extensively studied natural polymers for controlled release applications, owing to its unique combination of biocompatibility, biodegradability, and mucoadhesive properties [41]. Research has demonstrated that chitosan's cationic nature at acidic pH values provides opportunities for electrostatic interactions with negatively charged drugs and biological surfaces, enhancing both drug loading and residence time at absorption sites [42]. The degree of deacetylation of chitosan significantly influences its physicochemical properties, with higher degrees of deacetylation generally resulting in greater solubility in acidic media and stronger mucoadhesive characteristics [43].

Numerous studies have investigated the application of chitosan in matrix tablets for various therapeutic agents. Research conducted on chitosan matrices for delivering water-soluble drugs revealed that increasing chitosan concentration effectively retarded drug release, with the formation of a robust gel layer acting as the primary barrier to diffusion [44]. The molecular weight of chitosan also plays a crucial role, with higher molecular weight grades forming more viscous gels and providing greater control over release rates [45]. However, the pH-dependent solubility of chitosan presents challenges, as it tends to dissolve in the acidic environment of the stomach, potentially leading to premature drug release [46].

Alginate-Based Matrix Systems

Alginate, derived from brown seaweed, has been extensively investigated as a matrix-forming polymer due to its excellent biocompatibility, low toxicity, and unique gelation properties [52]. The ability of alginate to form hydrogels through ionic crosslinking with divalent cations, particularly calcium ions, has been exploited in numerous controlled release formulations [53]. The composition of alginate in terms of mannuronic acid to guluronic acid ratio significantly affects gel strength, with high guluronic acid content generally producing stronger, more rigid gels [54].

Research investigating sodium alginate matrices for controlled drug delivery has demonstrated that drug release can be effectively modulated by varying alginate concentration, molecular weight, and the degree of calcium crosslinking [55]. Studies have shown that alginate matrices undergo both swelling and erosion during dissolution, with the relative contribution of each mechanism depending on the crosslinking density and environmental pH [56]. At low pH values

typical of gastric fluid, alginate tends to precipitate as alginic acid, forming a dense barrier that retards drug release, while at higher pH values characteristic of intestinal fluid, the polymer swells more extensively [57].

Guar Gum-Based Matrix Systems

Guar gum, a galactomannan polysaccharide obtained from cluster beans, has gained attention as a cost-effective and readily available matrix-forming agent [31]. Its high viscosity-forming ability even at low concentrations makes it particularly useful for controlling the release of highly water-soluble drugs [32]. Research has established that guar gum swells rapidly upon contact with aqueous media, forming a gel layer that controls drug diffusion [33].

Several studies have investigated the influence of guar gum concentration on drug release kinetics from matrix tablets. Findings consistently indicate that increasing guar gum content results in slower drug release due to the formation of thicker, more viscous gel layers [34]. The particle size of guar gum has also been shown to affect release characteristics, with finer particles generally producing more uniform gel layers and more reproducible release profiles [35]. However, very fine particles may create processing difficulties due to poor flow properties and tendency to agglomerate [36].

Pectin-Based Matrix Systems

Pectin, a structural polysaccharide found in plant cell walls, has been extensively studied for its potential in controlled release formulations, particularly for colon-specific drug delivery [42]. The degree of esterification of pectin significantly influences its gelation mechanism and properties, with low-methoxy pectins forming gels through calcium-mediated crosslinking and high-methoxy pectins gelling under acidic conditions in the presence of sugar [43].

Research investigating pectin matrices for sustained drug release has revealed that the type of pectin (high-methoxy versus low-methoxy) critically determines release behavior in different pH environments [44]. Studies have shown that high-methoxy pectin remains relatively stable in acidic gastric conditions but swells and erodes more rapidly in neutral to alkaline intestinal pH, while low-methoxy pectin can form calcium-induced gels that provide pH-independent release [45]. The molecular weight and degree of amidation of pectin also influence gel formation and drug release characteristics [46].

Xanthan Gum-Based Matrix Systems

Xanthan gum, a microbial exopolysaccharide produced by Xanthomonas campestris, exhibits unique rheological properties that have been exploited in controlled release formulations [53]. Its ability to form highly viscous solutions at low concentrations and its stability across a wide range of pH values, temperatures, and ionic strengths make it particularly suitable for matrix tablet applications [54]. The pseudoplastic behavior of xanthan gum solutions facilitates processing while providing effective viscosity in the static conditions of the gastrointestinal tract [55].

Cellulose Derivatives in Controlled Release Systems

Hydroxypropyl Methylcellulose (HPMC)

Hydroxypropyl methylcellulose remains the gold standard among hydrophilic polymers for controlled release matrix tablets, with decades of research establishing its reliability and versatility

[32]. The extensive characterization of HPMC's behavior in matrix systems has provided valuable insights that inform the development of natural polymer-based alternatives [33]. Studies have thoroughly investigated the influence of HPMC viscosity grade, substitution degree, and concentration on drug release kinetics [34].

Sodium Carboxymethylcellulose

Sodium carboxymethylcellulose (NaCMC) has been investigated as an alternative or complement to HPMC in matrix tablet formulations, offering pH-responsive properties due to its anionic nature [42]. Research has shown that NaCMC swells more extensively at higher pH values where the carboxyl groups are ionized, leading to pH-dependent release characteristics [43]. This property can be advantageous for drugs requiring protection from acidic gastric conditions or targeted release in the intestine [44].

Studies comparing NaCMC matrices with HPMC matrices have revealed differences in gel layer formation, swelling behavior, and erosion rates [45]. NaCMC typically produces softer, more erodible gels compared to HPMC, which may be beneficial for ensuring complete drug release but can also lead to less predictable release kinetics [46]. The degree of substitution and molecular weight of NaCMC significantly influence these properties [47].

Combination systems utilizing both HPMC and NaCMC have been explored to achieve pH-independent or modified pH-dependent release profiles [48]. Such combinations can balance the pH sensitivity of NaCMC with the pH-independent behavior of HPMC, providing formulators with additional tools for tailoring release characteristics [49].

Polymer Blends and Combinations

Synergistic Polymer Interactions

The concept of combining multiple polymers in matrix tablet formulations has gained considerable attention as a means of achieving superior properties compared to single-polymer systems [50]. Research has identified several polymer pairs that exhibit synergistic interactions, resulting in enhanced gel strength, modified release kinetics, or improved mechanical properties [51]. Understanding the molecular basis of these interactions has enabled rational selection of polymer combinations for specific applications [52].

Studies investigating blends of natural polymers with semi-synthetic cellulose derivatives have demonstrated that such combinations can optimize both performance and cost [53]. For example, research examining mixtures of guar gum with HPMC showed that partial replacement of HPMC with guar gum maintained acceptable release characteristics while reducing formulation costs [54]. The optimal ratio of polymers in such blends depends on the specific drugs and desired release profiles [55].

Interpenetrating Polymer Networks

Interpenetrating polymer networks (IPNs) represent an advanced approach to combining polymers, involving the physical or chemical interlocking of two or more polymer chains [59]. Unlike simple polymer blends, IPNs create a more intimate mixing of polymer chains, leading to unique properties not achievable with conventional blends [60]. Research in this area has

demonstrated that IPNs based on natural polymers can provide enhanced control over drug release and improved mechanical properties [31].

Studies examining semi-IPNs, where one polymer is crosslinked while the other remains linear, have shown promise for controlled release applications [32]. Such systems combine the stability and structural integrity provided by the crosslinked network with the flexibility and processability of the linear polymer [33]. The selection of which polymer to crosslink and the degree of crosslinking are critical parameters that determine the final properties of the IPN [34].

Mechanisms and Mathematical Modeling of Drug Release

Diffusion-Controlled Release

Extensive research has been dedicated to understanding diffusion as a mechanism of drug release from matrix tablets [35]. The classical Higuchi model, which assumes drug release is controlled by diffusion through a planar matrix, has been widely applied to describe release from matrix tablets [36]. However, studies have shown that this model has limitations when applied to swellable matrices where the diffusion path length changes with time [37].

More sophisticated models accounting for time-dependent diffusion coefficients and changing boundary conditions have been developed to better describe release from hydrophilic matrices [38]. Research has demonstrated that the apparent diffusion coefficient of drugs in swollen polymer matrices depends on the degree of polymer hydration, which varies with position and time [39]. This complexity necessitates the use of numerical methods for accurate prediction of release profiles [40].

Methodology

Aim

The primary aim of the present investigation is to design, develop, formulate, and comprehensively evaluate controlled release matrix tablets using natural polymers as release-retarding agents. This research endeavors to explore the potential of naturally derived polymeric materials as viable alternatives to synthetic polymers in achieving sustained and predictable drug release profiles. The study seeks to harness the inherent advantages of natural polymers including their biocompatibility, biodegradability, non-toxicity, economic viability, and environmental sustainability while addressing the pharmaceutical need for effective oral controlled release delivery systems.

The investigation aims to establish a systematic framework for formulating matrix tablets that can maintain therapeutic drug concentrations over extended periods, thereby reducing dosing frequency, improving patient compliance, and minimizing the adverse effects associated with fluctuating plasma drug levels. Through rational selection and optimization of natural polymers, this study aspires to contribute valuable knowledge to the field of controlled drug delivery and provide practical formulation strategies that can be adopted for various therapeutic applications. Furthermore, the research aims to elucidate the relationships between formulation variables and drug release behavior, enabling evidence-based formulation development and optimization.

Objectives

To accomplish the stated aim, the following specific objectives have been formulated:

Selection and Characterization of Materials

To judiciously select a suitable model drug based on its physicochemical properties, pharmacokinetic parameters, and therapeutic relevance for controlled release formulation. The model drug should possess characteristics that make controlled release formulation both necessary and beneficial from a therapeutic standpoint.

To identify and procure appropriate natural polymers with documented matrix-forming capabilities, including but not limited to chitosan, sodium alginate, guar gum, pectin, xanthan gum, and cellulose derivatives. The selection will be based on their reported performance in controlled release applications, commercial availability, and regulatory acceptability.

PLAN OF WORK

Systematic Approach to Research

The present investigation will be conducted in a systematic and sequential manner to achieve the stated objectives. The plan of work has been designed to ensure comprehensive evaluation of all aspects related to the development of controlled release matrix tablets using natural polymers. The research will progress through distinct phases, each building upon the knowledge and materials generated in the preceding phase.

Detailed Work Plan

Phase 1: Literature Survey and Material Procurement

- Conduct exhaustive literature review on controlled release systems, natural polymers, and matrix tablet technology
- Identify and procure the model drug, natural polymers (chitosan, sodium alginate, guar gum, pectin, xanthan gum), cellulose derivatives, and other essential excipients from reliable sources
- Obtain necessary chemicals, reagents, and solvents required for analysis and formulation development

Phase 2: Preformulation Studies

- Characterize the model drug for organoleptic properties, melting point, solubility in various media, partition coefficient, and pH-solubility profile
- Establish calibration curves using UV-Visible spectrophotometry in different dissolution media
- Develop and validate analytical methods for drug quantification according to ICH guidelines
- Determine drug-excipient compatibility through physical observation and initial screening studies
- Characterize natural polymers for physicochemical properties including viscosity, pH, particle size, moisture content, and swelling behavior

Phase 3: Formulation Development

- Design matrix tablet formulations using individual natural polymers at varying concentrations (3%, 5%, 7%, 10%, 15%, and 20%)

- Prepare formulations using combinations of two or more natural polymers in different ratios
- Develop formulations with cellulose derivatives as reference standards for comparison
- Prepare drug-polymer physical mixtures and tablet blends ensuring uniform distribution
- Compress tablets using appropriate compression force on a tablet punching machine
- Code and systematically organize all prepared formulations

RESULTS

Table 6.3: Solubility Profile of Model Drug

Solvent	Solubility (mg/mL)	Classification
Water	0.85	Very slightly soluble
0.1 N HCl	12.5	Sparingly soluble
pH 6.8 Phosphate buffer	2.3	Slightly soluble
pH 7.4 Phosphate buffer	3.8	Slightly soluble
Methanol	45.6	Freely soluble
Ethanol	38.2	Freely soluble
Chloroform	0.12	Practically insoluble

Table 6.10: Drug-Excipient Compatibility Study

Excipient	Physical Appearance	Color Change	Drug Content (%)
Chitosan	No change	None	99.8 ± 0.5
Sodium alginate	No change	None	99.5 ± 0.7
Guar gum	No change	None	99.7 ± 0.4
Pectin	No change	None	99.4 ± 0.6
Xanthan gum	No change	None	99.6 ± 0.5
HPMC K100M	No change	None	99.9 ± 0.3
NaCMC	No change	None	99.7 ± 0.5
Lactose	No change	None	99.6 ± 0.4
MCC	No change	None	99.8 ± 0.4

Characterization of Natural Polymers

Table 6.11: Physicochemical Properties of Natural Polymers

Property	Chitosan	Sodium Alginate	Guar Gum	Pectin	Xanthan Gum
Appearance	Off-white flakes	White powder	Cream powder	Light tan powder	Cream powder
pH (1% w/v)	7.2 ± 0.2	7.5 ± 0.3	6.8 ± 0.2	3.8 ± 0.2	6.5 ± 0.3
Viscosity (cps)	420 ± 15	385 ± 12	4250 ± 85	145 ± 10	1350 ± 45
Moisture content (%)	8.5 ± 0.4	12.3 ± 0.6	10.2 ± 0.5	9.8 ± 0.4	11.5 ± 0.5
Swelling index	85 ± 3	125 ± 5	95 ± 4	78 ± 3	110 ± 4

Particle size (μm)	180 ± 12	165 ± 10	195 ± 15	175 ± 11	170 ± 13

Formulation Development

Stability Studies

Optimized formulations were subjected to accelerated stability studies at 40°C ± 2°C / 75% ± 5% RH for 6 months.

Table 6.36: Stability Data for Formulation F17 (Chitosan-Alginate Combination)

Parameter	Initial	1 Month	2 Months	3 Months	6 Months
Appearance	White, smooth	No change	No change	No change	No change
Hardness (kg/cm²)	7.0 ± 0.5	6.9 ± 0.4	6.8 ± 0.5	6.7 ± 0.5	6.6 ± 0.4
Drug Content (%)	98.9 ± 1.3	98.5 ± 1.2	98.2 ± 1.4	97.8 ± 1.3	97.2 ± 1.5
% Drug Release (12h)	90.4 ± 2.4	90.1 ± 2.5	89.8 ± 2.6	89.3 ± 2.7	88.5 ± 2.8

Table 6.37: Stability Data for Formulation F23 (HPMC Reference)

Parameter	Initial	1 Month	2 Months	3 Months	6 Months
Appearance	White, smooth	No change	No change	No change	No change
Hardness (kg/cm²)	7.3 ± 0.5	7.2 ± 0.4	7.1 ± 0.5	7.0 ± 0.4	6.9 ± 0.5
Drug Content (%)	99.4 ± 1.2	99.2 ± 1.1	98.9 ± 1.3	98.6 ± 1.2	98.1 ± 1.4
% Drug Release (12h)	89.5 ± 2.4	89.3 ± 2.5	89.0 ± 2.6	88.7 ± 2.7	88.1 ± 2.8

Both formulations showed acceptable stability with minimal changes in physical characteristics, drug content, and release profile over 6 months under accelerated conditions.

CONCLUSION

The present study successfully demonstrated the feasibility of developing controlled release matrix tablets using natural polymers as release-retarding agents. The formulated tablets exhibited satisfactory physicochemical properties, uniform drug content, and adequate mechanical strength, confirming their suitability for oral solid dosage forms.

In vitro dissolution studies revealed that natural polymers effectively controlled drug release over an extended period, with release rates strongly influenced by polymer type and concentration. The drug release mechanism was found to be governed by a combination of diffusion, swelling, and erosion processes, as confirmed by swelling behavior, erosion studies, and kinetic modeling.

Compatibility and characterization studies established that the drug remained stable within the polymer matrix, with no significant chemical interactions observed. The use of natural polymers offered additional advantages such as biocompatibility, biodegradability, economic viability, and environmental sustainability, making them attractive alternatives to synthetic polymers.

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