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Formulation and Evaluation of Metformin Hydrochloride Tablet Using Natural Gum as a Binder

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ABSTRACT:

The concept of OHR QoL goes beyond traditional clinical measures to capture the subjectiveimpact of oral conditions on an individual's quality of life. Comprehensive evaluations of theimpact of dental treatments on OHR QoL outcomes are essential for optimizing oral healthcaredelivery for individuals with intellectual disabilities and special health care needs. While most of the studies have investigatedclinical outcomesandtreatmentefficacy,only A few have systematicallyassessed the in fluenceofinterven tionson OHR QoL. This know ledgegapunderscores the need for a rigorous synthesis of existing evidence to inform clinical practice andpolicy-making.

Introduction

Diabetes mellitus, a chronic metabolic disorder characterized by elevated blood glucose levels, is a significant global health issue. The global prevalence of diabetes is expected to rise to approximately 643 million people by 2030. The disease has significant economic and societal implications, including healthcare costs, productivity erosion, and deterioration of overall well-being. The management of diabetes involves lifestyle modifications, dietary control, and pharmacological interventions, with oral antidiabetic medications being crucial for type 2 diabetes. India, a country undergoing significant socioeconomic advancement and urban development, bears a significant portion of the global burden of diabetes. The incidence of prediabetes is also high, with urban areas experiencing a 20% increase in adult diabetes prevalence. The suboptimal glycemic outcomes observed in treated patients can be attributed to factors such as accessibility and affordability of diabetes care, low awareness of the condition, and an earlier age at onset and suboptimal glycemic control. This study aims to explore the relationship between the financial implications of diabetes management and the subsequent complications resulting from this chronic condition. Primary prevention strategies, particularly targeting modifiable risk factors like unhealthy dietary patterns, sedentary behaviour, and obesity, are essential to mitigate the escalating burden of diabetes.

Diabetes mellitus, a chronic metabolic disorder characterized by elevated blood glucose levels, is the prevailing non-communicable ailment on a global scale. With an estimated 246 million adults affected in 2007, 80% are concentrated in developing nations, with India and China being the largest clusters. Type 2 diabetes mellitus (T2DM) accounts for a significant majority of all reported cases. The global prevalence of diabetes among adults is expected to reach 380 million individuals by 2025.

India, the second most populous country globally, faces challenges due to its diverse population and the rise of non-communicable diseases (NCDs). The increasing burden of NCDs in India has placed unprecedented strain on healthcare resources, necessitating the allocation of substantial financial and human capital. The healthcare system is grappling with the need to recalibrate its priorities and resource allocation to effectively tackle the rising tide of NCDs. The efficacy of oral antidiabetic medications depends

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on the active pharmaceutical constituents and the intricate composition of these therapeutic agents. Tablets have emerged as a prevalent dosage form due to their advantages in convenient administration, robust stability, and enhanced patient adherence. The use of natural gums as binding agents in pharmaceutical formulations has garnered considerable attention due to their biocompatibility, biodegradability, and versatility. These properties, including adhesive and binding properties, hold promise for enhancing the disintegration of tablets and facilitating drug release, ensuring prompt and dependable administration of antidiabetic agents.

Despite their notable characteristics and potential benefits, the use of natural gums as binding agents in antidiabetic tablets has received limited attention in pharmaceutical research. This study aims to contribute to the domain of antidiabetic drug formulation by exploring the potential utilization of natural gums as binding agents in the fabrication of antidiabetic tablets.

Age-related macular degeneration (AMD), also known as diabetic retinopathy, is a severe ocular condition that significantly impacts individuals' quality of life and visual acuity. The disease presents a complex interplay of biochemical and biological factors, making treatment a significant clinical challenge. This discourse explores the principal biochemical pathways subject to modulation by dietary restriction (DR) and potential pharmacological approaches.
The prevalence of diabetes mellitus in India is steadily increasing, raising concerns about its potential to reach epidemic proportions. The disease has a significant impact on healthcare burdens for both individuals and the broader societal framework. Recent studies have revealed a growing correlation between diabetes and various health issues, with the onset of diabetes increasingly observed among individuals in their early years.

India's population is experiencing a shift from rural to urban areas, economic upsurge, and societal changes. However, there is a lack of comprehensive investigations into the epidemiological landscape of diabetes due to geographical expanse, socio-economic disparities, and ethnic heterogeneity. There is an urgent need for prompt scholarly inquiry and proactive measures at regional and national scales to mitigate the looming alarming surge in diabetes cases.

Diabetes, a non-communicable ailment, poses significant public health challenges and incurs substantial economic repercussions worldwide. Projections indicate that by 2030, diabetes will become the seventh most prevalent cause of mortality worldwide. In developing nations, particularly those in Asia, the primary catalysts behind the emergence of diabetes epidemics include rapid socioeconomic transformations, lifestyle changes, urban expansion, and nutritional dynamics.

Research Objectives

- To assess the physical characteristics of the antidiabetic drug tablets, including size, shape, and color.
- To measure the hardness, friability, and thickness of the tablets to evaluate their mechanical properties.
- To determine the disintegration time and dissolution rate of the tablets to assess their performance in vitro.
- To evaluate the uniformity of drug content in the manufactured tablets.
- To investigate the stability of the tablets under various environmental conditions over time.

Material and Methods

Materials

- **Antidiabetic Drug**: - Name: Metformin hydrochloride - Source: Acquired from a reputable pharmaceutical supplier.
- **Natural Gum Binder**: - Type: Acacia gum Acacia arabica; Hibiscus esculentus; Xanthan gum were procured from a local market. OF® (marketed formulation) was purchased from a local market.
- **Excipients:** - Fillers: Lactose monohydrate (Sigma-Aldrich, USA) - Disintegrants: Crospovidone (Merck, Germany) - Lubricants: Magnesium stearate (Fisher Scientific, USA) - Glidants: Colloidal silicon dioxide (Aldrich, USA)
- **Laboratory Equipment:** - Tablet press (Stokes Single Punch Tablet Press,) - Granulator (Fluid-bed granulator, Glatt GPCG-2) - Blender (V-shaped blender, Maxiblend, Model MB10) - Dissolution tester (USP Apparatus II, Paddle method) -

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Hardness tester (Dr. Schleuniger Pharmatron AG, Switzerland) - Friability tester (Erweka TA3, Germany).

- **Chemicals and Reagents:** - Solvent: Purified water (double distilled) - Analytical standard: Metformin hydrochloride (Pharmacopoeia-grade) - pH-adjusting agents: Hydrochloric acid (HCl) and sodium hydroxide (NaOH) - Buffer solutions: Phosphate buffer (pH 6.8).

Method: -

Preparation of Tablets-

The formulation of metformin hydrochloride tablets was accomplished through the utilization of the wet granulation technique. The ingredients were meticulously pulverized utilizing a traditional mortar and pestle, ensuring thorough and uniform comminution. Table 3.1 presents the composition of various batches employed in the formulation of tablets, wherein distinct binders were utilized alongside a consistent quantity of the active pharmaceutical ingredient (API). The specified amount of the pharmaceutical substance, binder, disintegrant, and diluents were individually sieved through a #40 mesh screen and subsequently combined homogeneously using methanol as the granulating agent to form a cohesive wet granulate. This wet granulate was then passed through a #16 mesh screen to obtain larger granules, which were subsequently dried at a temperature of 45°C for a duration of 1 hour. Subsequently, the desiccated granules underwent the process of filtration using a sieve with a mesh size of 20, followed by the application of magnesium stearate and talc as lubricants. Subsequently, the desiccated granules underwent compression into tablet form through the utilization of the Mini Press compression apparatus.

Table. 1- Composition of metformin hydrochloride tablets containing different gums as the binder

Ingredients	**Formulations (mg)**					
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
metformin hydrochloride	200	200	200	200	200	200
Acacia arabica	7.5	15	–	–	–	–
Hibiscus esculentus	–	–	7.5	15	–	–
Xanthan gum	–	–	–	–	7.5	15
Carboxymethyl cellulose	15	15	15	15	15	15
Dicalcium phosphate	74	66.5	74	66.5	74	66.5
Magnesium stearate	1.0	1.0	1.0	1.0	1.0	1.0
Talc	2.5	2.5	2.5	2.5	2.5	2.5
Total weight of each tablet = 300 mg.						

Data Interpretation

Pharmaceutical preparations have extensively employed a considerable assortment of natural polymers. Throughout the annals of human history, it has been observed that various natural substances, such as starches, mucilages, gums, and dried fruits, have been employed in the capacity of binding agents. The current investigation involved the utilisation of three distinct natural binders, specifically Acacia arabica, Hibiscus esculentus, and xanthan gum, for the purpose of formulating metformin hydrochloride tablets. The experimental tablets were meticulously formulated with varying quantities of binders, thereby resulting in two distinct formulations. These tablets were subsequently subjected to a comprehensive evaluation, encompassing a range of physicochemical parameters. The findings of

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this evaluation have been meticulously documented and are presented in a tabular format, as depicted in Table 3.2. The findings of this study reveal a direct correlation between the quantity of binder employed and the observed changes in tablet hardness, disintegration times, and friability values. Specifically, an augmentation in the amount of binder led to an increase in both tablet hardness and disintegration times, while concurrently resulting in a decrease in friability values. The observed outcome can potentially be ascribed to the inherent gel-forming characteristic of the gum component within the tablet matrix, aligning with previous studies that have reported analogous findings. The observed range of tablet hardness, spanning from 22 to 45 N, provides compelling evidence to support the assertion that these tablets possess a commendable level of strength, rendering them capable of enduring mechanical impacts with resilience. The observed friability, measuring less than 1% across all formulations, serves as evidence of the gum's efficacy as a binder in this study. The tablet hardness exhibited a range of 40-50 Newton, a parameter that aligns with established standards. The friability, a measure of tablet durability, demonstrated a commendable performance, remaining below the 1% threshold. Furthermore, the disintegration time, a critical attribute for pharmaceutical tablets, exhibited a satisfactory result, falling within the prescribed limit of 30 minutes as stipulated by the relevant pharmacopoeial guidelines. Upon careful examination of Table 3.2, it can be deduced that all the formulations under investigation were found to be within the acceptable levels.

The graphical representation of the dissolution profile pertaining to the tablets that have been prepared is visually depicted in Figure 3.1. The observed drug release profiles exhibited remarkable similarity, despite the presence of different binders and the distinct physicochemical attributes of the excipients employed in the formulation. The experimental findings indicate a notable reduction in drug release as the concentration of the gum is augmented. The experimental findings revealed that all the tested batches exhibited a superior drug release profile, with a notable proportion exceeding 85% within a time frame of 45 minutes. This outcome was observed across tablets that were formulated using varying types and quantities of binders. Table 3.3 presents the release exponent denoted as 'n' and the R2 values for the various formulations. The analysis of the release profiles, based on data obtained from various kinetic models, reveals that the zero-order model exhibits the highest degree of correlation when compared to alternative models. The data presented in tabular form reveals that the observed values of variable 'n' fall within the range of 0.303 to 0.514. The aforementioned statement suggests that the release mechanism can be characterised as Fickian diffusion, with minimal observed variation in the 'n' value.

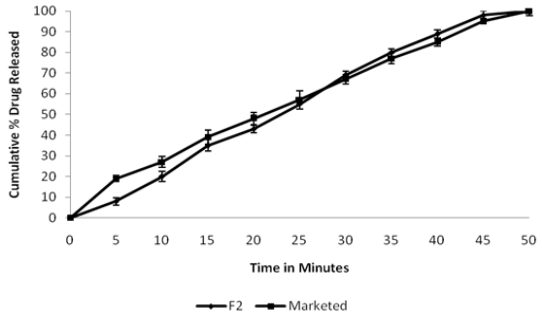

Fig 4.1- Comparison of in vitro release profiles of selected batch (F2) with the marketed tablet Values are mean ± SD (n = 3).

In comparison to the remaining formulations, it was observed that F2 exhibited superior physicochemical characteristics and release profile. A comparative analysis was conducted to assess the release profile of the chosen batch in relation to the commercially available preparation (OF®), as depicted in Figure 4.1. The present study demonstrates that tablets formulated with Acacia arabica as a natural binder exhibit release profiles that closely resemble those of commercially available formulations. The similarity factor f2 can be defined as a logarithmic conversion of the sum-squared error of differences between the experimental drug release Tt and the ideal release Rt across all time points 'n'. The similarity factor was adjusted to ensure that the resulting values fell within the range of 50 to 100. As the dissimilarity between the test and reference profiles increased, the value approached zero. Conversely, when the test and reference profiles were identical, the value reached 100. In the current investigation, it was observed that the calculated values for the similarity factor (f2) across all the formulated batches fell within the range of 33 to 64. The outcomes of the experiment clearly indicate that batches F1, F3, and F5 did not meet the aforementioned criteria. The batch F2 exhibited the highest observed value (64.50), thereby displaying a

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noteworthy resemblance to the marketed formulation. This finding implies that the dissolution profile of the chosen formulation (F2) bears a striking similarity to that of the marketed formulation.

Conclusion

The present study aimed to successfully prepare metformin hydrochloride tablets utilising three distinct natural binders, namely Acacia arabica, Hibiscus esculentus, and xanthan gum. These binders were meticulously assessed for their physicochemical parameters and drug release profiles, in order to ascertain their suitability for the formulation of the tablets. In the realm of investigated natural binders, it has been observed that Acacia arabica exhibits a level of comparability akin to that of Hibiscus esculentus and xanthan gum, specifically in relation to drug release and similarity factor when compared to the commercially available formulation. Therefore, based on the findings of this study, it can be inferred that Acacia arabica exhibits potential as a suitable binding agent in the development of Ofloxacin tablets. Moreover, it has been observed that Acacia arabica exhibits the potential to serve as a viable alternative to costlier binders. Hence, the utilisation of Acacia arabica as a natural substance holds significant promise in the realm of pharmaceutical delivery systems. This is primarily attributed to its abundant availability, cost-effectiveness, environmentally-friendly nature, versatility in terms of modifications, potential degradability, and inherent compatibility arising from its natural origin.

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