Fabrication of Excipients Free Tablet using Biodegradable Cellulose Paper

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***Abstract*- In this study, the potential for compressing cellulose paper into tablets was rigorously examined. Results demonstrated that paper may be utilized to make tablets, regardless of the type of paper used. The pills have a sleek, polished appearance. The pharmaceutical quality was satisfactory; all of the pills met the Indian Pharmacopeia's standards for tablets. Compressing drug-loaded paper resulted in the creation of drug-loaded tablets. The quality of the medication was unaffected by drug loading. However, the uncoated pills had a very quick disintegration rate, causing severe swelling when they came in contact with water, which could make it difficult for people to take them following oral administration. Tablets were effectively covered with a polymer film to prevent swelling, which not only prevented swelling but also caused a rapid disintegration in simulated gastric juice. In reality, paper-based tablets offer an innovative and promising method for enhancing oral medication delivery. According to the Indian Pharmacopeia, they can be simply synthesized without any additional excipients and have medicinal purity.**

***Index Terms*- Cellulose Paper, Paracetamol, SmartFilm Technology.**

INTRODUCTION

A drug is a chemical that is intended for use in the diagnosis, treatment, mitigation, or prevention of disease. Drugs are rarely administered in their pure chemical form but in their physical form, known as a dosage form, which makes them easier for humans to take and administer [1].

The most common technology for giving patients active pharmaceutical ingredients (API) orally is still solid dosage forms like tablets and capsules [2]. The convenience of administration, high patient compliance, and cost-effectiveness of tablets make them one of the most practical and favored oral dose forms [3]. Tablets are a traditional solid dosage form that has many advantages over other dosage forms. Tablets come in a variety of weights, sizes, and shapes based on the medication and the intended manner of administration [4]. Some medications have an ideal concentration window within which the greatest benefit is obtained. Dosages outside of this window can be hazardous or have no therapeutic effect at all, depending on the drug's dosages and dosages involved [5].

Up to 50–60% of all dosage forms are administered by oral methods, which are well accepted [6]. The use of thin films as an alternative to standard dosage forms has been noted. The films are easy to swallow, self-administrable, and have a quick-dissolving dose form. They are regarded as an adaptable platform for drug delivery because they are adaptable in shape and size [7]. Pharmaceutical companies are researching the benefits of giving patients access to their medication in pill form, instead of having to fill out a prescription for it with another dosage form like mouth freshener or contact lens strips [8]. An "immediate release" formulation is one that doesn't use galena adjustments to slow down the rate of drug release from the formulation or absorption. According to the FDA, an acceptable diluent or carrier can be used to facilitate immediate release in such a case [9]. In order to address poor solubility, a unique medication delivery mechanism was recently introduced. The so-called *SmartFilm* technique loads amorphous APIs into a matrix made of regular paper [10]. A typical paper-based product is composed of 90-99 percent cellulose fibers. They are the main structural elements and have the greatest impact on the final qualities. The chemical and physical properties of paper products are affected by a network of self-bonding cellulose fibers [11]. Starch is a readily available, low-cost, renewable, and biodegradable natural polymer. Synthetic and natural polymers can be mixed to greatly enhance the qualities

of each [12]. We are using paracetamol used as API. Paracetamol (an international name used in Europe) and acetaminophen (an international name used in the USA) are two official names of the same chemical compound derived from its chemical name: N-acetyl-para-aminophenol and N-acetyl-para-aminophenol [13]. It is commonly utilized in many pharmaceutical formulations and presentations that aim to maximize the usage of the medication by promoting effective absorption and minimizing side effects [14]. Although we strive to produce tablets without excipients, coating is occasionally essential. Applying a thin polymer-based film to a tablet or granule containing active medicinal ingredients is a common pharmaceutical process known as tablet coating (APIs). Coating solid dosage forms is done for a variety of reasons, but the main one is to regulate the release profiles [15].

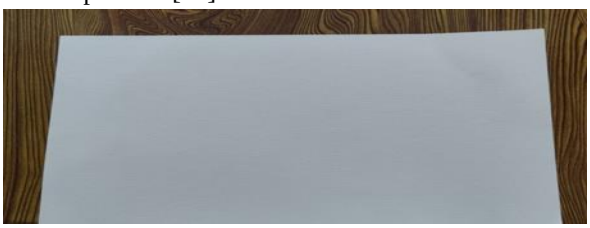


Figure 1: Cellulose Paper used for making Tablets

MATERIALS AND METHODS

A. Materials

Cellulose Paper is used as SmartFlim. We purchased this cellulose paper from e-commerce website and is manufactured by *Chee Wah Corporation Berhad, Malaysia*.

Paracetamol is used as the API and is incorporated in the cellulose paper.

Micro-Pipette was used for loading the API in the paper.

B. Methods:

Production of unloaded tablets:

Using a single punch tablet press and applying compression forces of around 30000 N, flat-faced, bevel-edged tablets with an unloaded mass of about 0.2 g and a diameter of 1 cm were created in the study's first section. Prior to compression, the various varieties of paper were divided into pieces, each with a mass of around 0.2 g. In this case, the height and the corresponding mass and volume were analyzed to roughly establish the paper's density. In order to manage the mass, the appropriate area of paper was determined, cut out, and weighed. The paper sheets were then divided into pieces that were around 1 cm x1 cm in size. The tablet press's cavity was manually filled with the resulting tiny bits of paper, and those pieces of paper were manually compressed. By implementing the tablet tests from the Indian Pharmacopeia 8.0, the qualities of the produced tablets were evaluated. [10].

Production of tablets loaded with API:

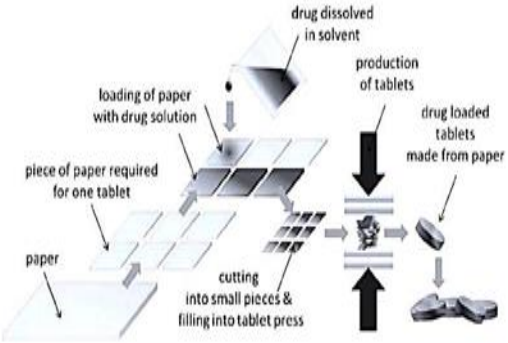


Figure 2: Production of Drug Loaded Tablets made from Paper

The creation of drug-filled tablets was the goal of the study's second section. As a model drug, paracetamol was employed. Describes the production process in detail. First, sheets of paper with a mass of around 0.2 g were cut into. Using a pipette, 0.00025 l of an aqueous paracetamol solution (0.02 g/l) was added to the sheets to load them with the medication. After the process had dried, it was carried out a total of 12 times, resulting in a load of 0.06 g of paracetamol per sheet of paper. The sheet was divided into tiny pieces, each measuring roughly 1 cm × 1 cm. Once more, the drug-loaded pieces of paper were manually inserted into the tablet press's cavity and squeezed. The properties of the drug-loaded tablets were assessed as described above. In addition, content uniformity and the drug release were investigated according to the Indian Pharmacopeia 8.0 [10].

EVALUATION PARAMETERS

A. Weight Variation:

The amount of fill in a tablet press determines the weight of a tablet. With the first few pills, the fill volume is adjusted to provide the required weight and content. A reliable indicator of the equivalent variation

in medication content is the weight variation of each individual tablet [16].

$$\text{Weight Variation (\%)} = \frac{\text{Weight of each tablet} - \text{Average weight of tablets}}{\text{Average weight of tablets}}$$

B. Hardness Testing:

Tablets need to be strong enough to endure mechanical manipulation during production, packaging, and delivery. By cracking the tablet between 2nd and 3rd fingers with the thumb acting as a fulcrum. If there is a sharp snap, the tablet is an acceptable strength. The amount of force needed to break a tablet in a diametric compression is referred to as the tablet's hardness. In this test, the tablet is sandwiched between two anvils, pressure is given to the anvils, and the amount of force needed to simply break the tablet is recorded as the crushing strength [16].

Instruments used: Monsanto Hardness Tester

Figure 3: Hardness Testing with Monsanto Hardness Tester

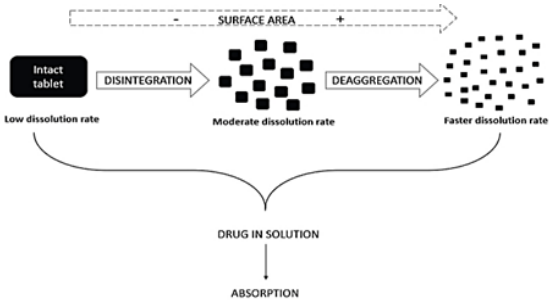


Figure 4: Disintegration Process

C. Friability testing:

Friability testing has gained widespread acceptance in the pharmaceutical sector. Testing determines how much mechanical stress tablets can take during production, distribution, and client handling. The Friabilator, or Friability Tester, is a tool used to assess the physical resistance of tablets to mechanical shock and wear [17].

A friability test can be performed to evaluate the ability of the tablets to withstand abrasion in handling, handling and transporting [18].

$$\text{Friability (\%)} = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Initial Weight}} \text{ X } 100\ \%$$

Instruments used: Roche Friabilator

C. Thickness Uniformity

Tablet thickness should be regulated at a specified value of 5% or less. Any difference in tablet thickness should not be visible to the untrained eye in order to retain customer approval and to make packing easier. Tablet thickness fluctuates with variations in die fill and tablet weight when compressive stress is constant. However, when the die fill remains constant, the thickness fluctuates depending on the compressive load [16].

Instrument: Vernier Calliper.

D. Disintegration testing:

A tablet's mechanical disintegration into smaller particles or granules, or the breakdown of the inter-particle connections created during tablet compaction of granulated particles of the active pharmaceutical ingredient (API) and excipients, is referred to as disintegration. Disintegration typically occurs in two stages: first, the tablet breaks down into small granules, and then disaggregation, or granule disintegration, occurs after the liquid wets the tablet surface and enters the pores. For the speed of the tablet's initial medication release, the first step is crucial. However, the gelling of a disintegrate slows down this procedure. If there was no disintegration, only the API at the compact's surface would disintegrate. A higher rate of dissolution is produced by the increased surface area compared to the entire tablet. Due to the increased surface area in contact with the medium in the second phase, as shown in the scheme, an even quicker drug dissolution rate is attained. To encourage dosage form (DF) disintegration when in contact with a fluid, disintegrates can be added to the formulation. These excipients frequently contain the D-F matrix, allowing for various methods of disintegration. The various tablet disintegration mechanisms are enumerated [19]. Disintegration time was seen as a crucial measure for determining the quality of conventional immediate-release tablets, particularly those used to treat chronic disorders that required a quick commencement of

action, such as hypertension and heart failure. All commercial tablets utilised in the study have good disintegration times, and the USP states that the maximum disintegration time for an uncoated tablet is 30 minutes (less than 15 min) [20].

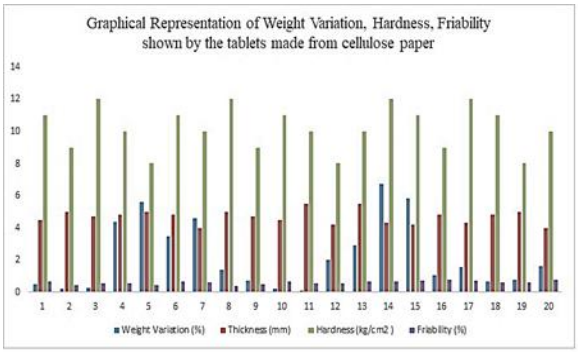
RESULTS & DISCUSSION

Results:

Table 1: Results of tests performed to assess the pharmaceutical quality of tablets according to Indian Pharmacopoeia (Physical Appearance, Weight Variation, Hardness, Friability, disintegration time).

Discussion:

Type of Paper	Physical Appearance	Weight Variation (%)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Disintegration Time
Cellulose Paper	Tablets look almost similar to classical tablets being Composed of powder or granules.	0.49	4.5	11	0.63	All tablets Disintegrated within 15 min.
		0.23	5	9	0.41	
		0.27	4.7	12	0.54	
		4.35	4.8	10	0.57	
		5.63	5	8	0.44	
		3.46	4.8	11	0.64	
		4.61	4	10	0.6	
		1.38	5	12	0.4	
		0.74	4.7	9	0.48	
		0.23	4.5	11	0.67	
		0.1	5.5	10	0.52	
		2.02	4.2	8	0.56	
		2.91	5.5	10	0.65	
		6.73	4.3	12	0.66	
		5.84	4.2	11	0.71	
		1.03	4.8	9	0.77	
		1.54	4.3	12	0.72	
		0.65	4.8	11	0.59	
		0.78	5	8	0.6	
		1.63	4	10	0.76	



Each tablet has a smooth surface and resembles traditional uncoated tablets consisting of powder or granules in appearance. Production and evaluation of API-loaded tablets The initial phase of the project demonstrated that any sort of paper can be used to create tablets. The next stage was to determine whether drug-filled tablets could likewise be made from paper. As previously mentioned, Paracetamol was added to the various sheets, and the resulting drug-loaded films of paper were then diced up and compacted as previously mentioned. The results of the pharmaceutical tests, i.e. Physical Appearance, Weight Variation, Hardness, Friability, disintegration time are summarized in *Table 1*. Results confirm that all tablets fulfilled the criteria according to the Indian Pharmacopeia.

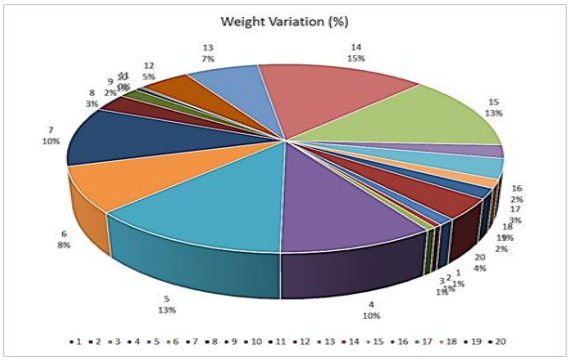
Weight Variation

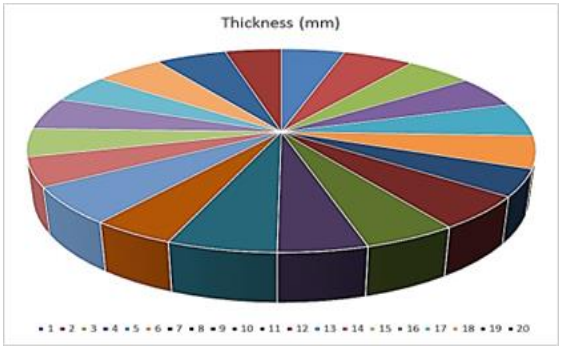
Here in this experiment, we got a weight variation of *784.15 ± 24.54* for tablets made from cellulose paper which is acceptable according to our reference paper.

Thickness:

In our experiment, we discovered the average thickness of the cellulose paper tablets as 0.46 cm which is in the range of I.P.

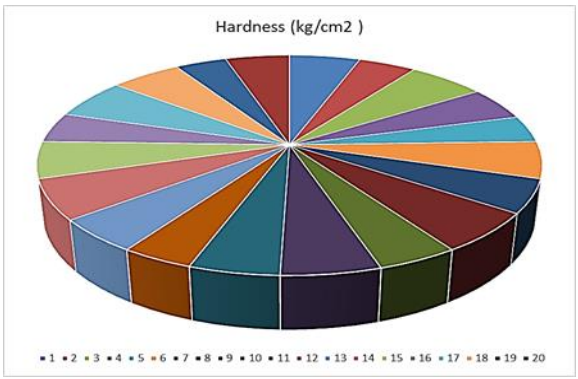
Figure 5: Tablets made from Cellulose Paper





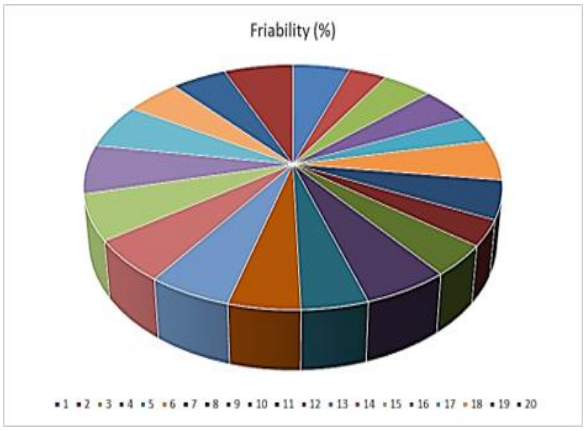
Hardness:

The tablets made from cellulose paper possess sufficient strength and breaks with an average pressure of *10.11 kg/cm^2*.



Friability:

Friability was determined according to test method in I.P. Here, we observe the friability loss of *0.55 ± 0.11* which is appropriate for the handling and transportation of the tablets.



Disintegration:

Disintegration was achieved within less 15 min. Disintegration started with a massive swelling of the tablets within 60 s. Within 2 min the volume of the tablet was already doubled and tripled after about 5 min. After 15 min the tablet was disintegrated, i.e. all paper was moist and soft.

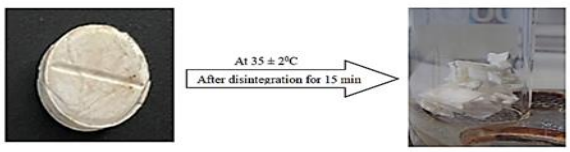


Fig-6: Disintegration

CONCLUSION

In our research, it has been concluded that the properties of all batches of paper tablets were Figure matched with the specifications with the I.P. The evaluated properties were weight variation, Hardness, friability, thickness, disintegration time of the tablet. The Analysis of the selected tablets in this study revealed that the tablets were manufactured in a satisfactory manner for the objectives. So we can conclude that the tablet made from paper is effective as per the requirements and thus can complement the regular tablets. The Indian Pharmacopoeia describes the tablets' physical appearance, weight variation, hardness, friability, and disintegration time as being almost identical to those of traditional tablets made of powder or granules. Paper-based drug-loaded tablets can be created by preloading the appropriate paper with an API. Compression forces are a key factor that affects the drug release profiles of paracetamol from the paper-based tablets. The kind of paper and level of hardness of the tablets had an impact on the caffeine release patterns. Paper-based tablets must be coated after compression to postpone the fast-disintegrating paper sheets' time of disintegration. The disintegration time was shown to be postponed by coating. It may be believed that coating converts tablets into simple, solid oral dose forms that are easy to swallow. Based on these findings, it is possible to draw the conclusion that paper-based tablets offer a cutting-edge, prospective drug delivery system—not only for the distribution of insufficiently soluble actives but also for the creation of customized pharmaceutical oral medicinal solutions.

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