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Development and Characterization of Enteric Coated Diclofenac Sodium Tablet

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Abstract

Tablets of the drug diclofenac sodium with an enteric coating are used to treat fever, discomfort, and inflammation. The pills are made to withstand the stomach's acidic environment while dissolving in the small intestine's alkaline environment. With this delayed release formulation, there is a lower chance of experiencing gastrointestinal adverse effects while also extending the duration of medication absorption and increasing medicinal efficacy. Enteric coated tablets are solid unit dose forms for oral administration that bypass the stomach and transport the medication straight to the small intestine. Given that the name "enteric" refers to the small intestine, enteric coatings prevent the release of medication before it reaches this organ. A coated surface that is stable at the stomach's very acidic pH is how most enteric coatings work.

Keywords: Diclofenac Sodium; Tablets; Nonsteroidal Anti-Inflammatory Medication

Introduction

Diclofenac sodium is a synthetic, nonsteroidal anti-inflammatory, and analgesic compound Figure 1.

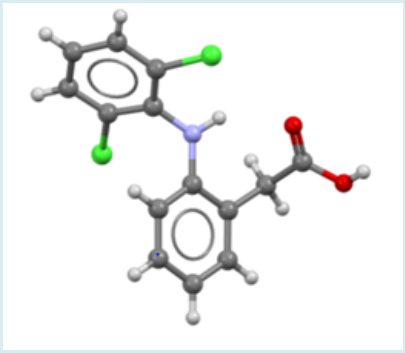

Figure 1: Structure of Diclofenac Sodium.

New chemical synthesis techniques and enhanced analytical and screening technologies have sparked the development of new nonsteroidal anti-inflammatory medication (NSAID) drugs in recent decades [1-5]. Recent developments in NSAID pharmaceutics have concentrated on the creation of solutions to deal with severe dose-dependent GI, CV, and renal adverse effects (AEs) related to the use of NSAIDs [6-13]. One of the most often used nonsteroidal anti-inflammatory medicines (NSAIDs), diclofenac (DCF), also known as 2-(2-((2,6-dichlorophenyl) amino) phenyl) acetic acid, has both antipyretic and analgesic characteristics [14]. Since 1974, research has shown that DCF is quite effective for treating rheumatic symptoms, acute joint inflammation, and mild to moderate pain [15].

Identification of Drug

Ultraviolet Spectroscopy

Using an appropriate medium, the samples were scanned for absorption maxima (max) in the 200–400 nm range by UV spectrophotometric analysis [16]. Fever, pain, and inflammation are treated with enteric-coated tablets of

the medication diclofenac sodium. The tablets are designed to survive the acidic environment of the stomach while dissolving in the alkaline environment of the small intestine. With this delayed release formulation, the risk of suffering gastrointestinal side effects is reduced, and the duration and effectiveness of drug absorption are both increased. Solid oral dosage forms called enteric coated tablets avoid the stomach and deliver medication directly to the small intestine. Considering that "enteric" is the name of the small intestine, before the medication reaches this organ, enteric coatings stop the release of the medication. Most enteric coatings function by stabilizing the coated surface at the extremely acidic pH of the stomach Figure 2.

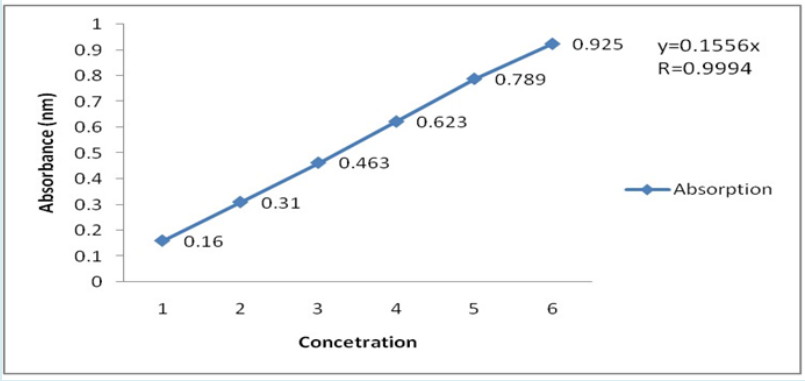

Figure 2: Standard graph of Diclofenac Sodium.

Development of NSAID and Diclofenac

Salicylic acid, a historically used therapeutic medicine made from the active ingredient in willow bark salicin, has antipyretic, analgesic, and anti-inflammatory actions. Salicylic acid was utilised globally in the late nineteenth century for a number of diseases .There was a need for new, better chemical derivatives of salicylic acid due to its bitter taste and accompanying gastrointestinal discomfort. In order to create a mildly acidic acetylsalicylic acid with a more pleasing taste, Felix Hoffman and Arthur Eichengrun acetylated the salicylic acid molecule in 1897. Bayer (Berlin, Germany) patented this compound as aspirin in 1899 [17-19].

The Geigy Corporation (Basel, Switzerland) produced a novel molecule with significant anti-inflammatory and uric acid excretion-promoting properties in the early 1950s. This substance created water-soluble salts of aminophenazone [20,21].

Excipient

1. Diluents, binders or granulating agents, glidents and lubricants to ensure efficient tableting;
2. Disintegrates: to promote tablet break up in the digestive tract;
3. Sweeteners or flavours: to enhance the taste;
4. Polymer coating: it is applied to make the tablet smoother and easier to swallow, to control the release rate of the active ingredient, to make it more resistant to the environment.

There are three methods by which tablets are manufactured;

- Wet granulation
- Dry granulation
- Direct compression

Wet Granulation

- It is most commonly used method for the manufacturing of tablets.
- Water is frequently used as the granulation fluid (and heat is employed to dry the formed granules), it is important to ensure that the therapeutic agent is chemically stable during the granulation process.
- The wet granulation exhibit sufficient mechanical properties to be subsequently exposed to other unit operations, Eg: film coating.
- Tablet quality is directly affected by the choice and concentration of binder and the type and volume of granulation fluid. Due to the number of unit operations to the required, the manufacture of tablets by wet granulation is not as efficient as other methods. Eg: direct compression.

Methodology

Preparation of Tablet

Diclofenac sodium was used as a model drug in the formulations, while HPMC 100 cps and NaCMC were used as

rate-controlling polymers Figure 3. Magnesium stearate or talc were utilised as lubricants, while lactose monohydrate was used as a compression assist. In all tests, all formulation ingredients other than magnesium stearate and talc were dry mixed and subsequently granulated by adding water Figure 4. Then a 20-mesh screen was used for wet screening.

Granules were dried for one hour at 50 C. The dried granules were lubricated by combining them with talc and magnesium stearate. A single-punch hand/motor-operated tablet press (Cadmach, Ahmedabad, India) equipped with 13-mm concave punches was used to compress the tablets Figure 5. Lists the several formulations that were created together with information on their compositions, hardnesses, and average weights [22] Figure 6.

Preparation of Granuals

The wet granulation process involves several steps, including

Figure 3: weighing of Ingredient.

Weighing and mixing of formulation ingredient

Figure 4: Mixing of the powders or granules with other excipients.

Preparing the dump mass

Figure 5: Sizing the granulation by Wet screening.

Wet screening/Screening the damped powder into pellets or granuals

Figure 6: Granules.

Drying of moist granuals

Sizing the granulation by dry screening

Lubrication of granuals.

The preparation of the granulation mixture involves blending the active pharmaceutical ingredient with excipients such as binders, fillers, and lubricants. After the powder mixture is wetted with a binder solution, it is mixed to form a wet mass. The wet mass is then passed through a wet screen to break down any large aggregates before being dried. Finally, the dried granules are screened to obtain the desired particle size range.

Manufacture of Tablets Steps:

- Mixing of the therapeutic agents with the excipients
- Granulation of the mixed powders (this is not performed in direct compression)
- Mixing of the powders or granules with other excipients (mostly lubricants)
- Compression into tablets
- The details of each of these steps will vary depending on the manufacturing method used Figure 7.

Figure 7: Automatic compression machine.

Method of Tablet Coating

One thousand millilitres (ml) of distilled water was weighed into a mixing bowl and swirled to create a vortex. A gentle, continuous stream of 300 g of Cellulose acetate phthalate white powder was introduced to the liquid vortex's centre, preventing clumping and preserving the vortex. The mixing process went on for another 20 to 25 minutes. A 250 m screen was used to filter the cellulose acetate phthalate aqueous dispersion before the coating procedure began. Throughout the coating procedure, the aqueous enteric coating dispersion was kept under constant stirring. Both coating dispersions were made in accordance with Colorcon's technical specifications and instructions [23].

Methodology of Entric Coating

A standard coating pan and one spray gun were used to coat the tablets. Alcohol 95% was formerly used to clean the coated pan. Diclofenac sodium core tablets in a batch size of 100 mg were chosen for coating. The coating pan was filled with the core tablets. Using a drier and air compressor tablet cores were pre-heated to a temperature of roughly 40 °C. Throughout the whole coating operation, warm air (up to 50–55°C) was blown into the coating pan. Cellulose acetate phthalate aqueous dispersionu was used in the spray cannon, which was operating at the correct flow rate.

Seal coating dispersion was sprayed into the moving pan. In the coating pan for minutes. After coating with Cellulose acetate phthalate, the core pills increased in weight by 102 percent. The coating conditions and parameters are listed in Tables 1 and Table 2 [23].

Ingredient	Formulations (mg)				
	F1	F2	F3	F4	F5
Diclofenac Sodium	37.5	37.5	37.5	37.5	37.5
Cellulose Microcrystalline	31	30.75	30.75	32	30.75
Magnesium Stearate	4.35	4	4	3.5	3.5
Mannitol	51.25	51	52	52.1	53.1
Lactose	8.25	9.1	8.1	7.25	7.5
Cellulose acetate phthalate	20	20	20	20	20
Total weight	152.35	152.35	152.35	152.35	152.35

Table 1: Ingredient of Tablet.

Evaluation Parameter	Formulations (mg)				
	F1	F2	F3	F4	F5
Weight Variation	0.52	0.3	0.41	0.49	0.53

Table 2: Weight variation.

Evaluation of Formulated Tablets

Weight Variation Test

Twenty tablets were weighed separately for the IP weight variation test, and the average weight was computed and compared to the weights of the individual tablets against the average [24] Figure 8.

Figure 8: Weight variation.

Friability Test

The laboratory friability tester (Roche Friabilator) uses a plastic container that rotates at 25 rpm while dropping the tablets at a distance of six inches with each revolution to test a variety of tablets to assess the combined effects of abrasion and shock. The friabilator is typically loaded with a pre-weighed tablet sample and run for 100 revolutions. The pills are then reweighed and dusted. Conventional compressed pills are often regarded as effective if they lose between 0.5 and 1% of their weight [24] Figure 9 and Table 3.

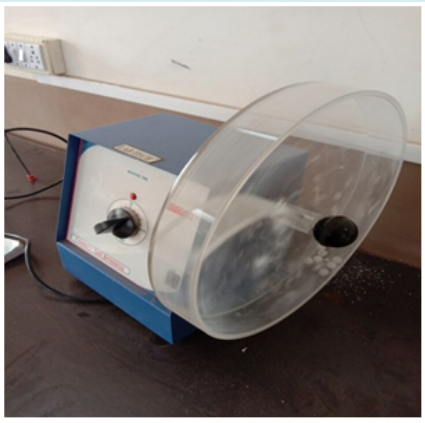

Figure 9: Friabilitor.

Evaluation Parameter	Formulations				
	F1	F2	F3	F4	F5
Friability Test	2%	0.47%	0.35%	0.60%	0.20%

Table 3: Friability Test.

Hardness Test

Tablet hardness was determined by Monsanto and Pfizer hardness tester Figure 10 and Figure 11. The reading was noted. The reading indicates the hardness of the tablet in kg/cm2 [25] Table 4.

Figure10: Monsanto.

Figure 11: Pfizer.

Evaluation Parameter	Formulations				
	F1	F2	F3	F4	F5
Hardness Test	6	4.50	3.50	5	4

Table 4: Hardness Test.

Tablet Size and Thickness

Along with weight variation that exceeds the permitted limitations, variations in tablet thickness and diameter may pose issues with counting and packing Figure 12 and Figure 13.

Figure 12: Diameter Test.

Figure 13: Thickness of Tablet.

Tablet diameter and thickness should be kept to within 5% of a defined value. Using a Vernier aliper, (china) the tablet's thickness and diameter were measure [25] Table 5 and Table 6.

Evaluation Parameter	Formulations (Cm)				
	F1	F2	F3	F4	F5
Diameter of Tablet	10	10.10	10.57	10.60	10.08

Table 5: Diameter Test.

Evaluation Parameter	Formulations (cm)				
	F1	F2	F3	F4	F5
Thickness Of Tablet	5	4.3	5.1	4	5.58

Table 6: Thickness of Tablet

Disintegration Time in Vitro

Six tablets were randomly chosen from each brand, one from each of the tubes in the basket-rack assembly of the disintegration device, and placed in each tube. At 370C, the assembly was placed in the artificial gastric fluid. After 120 minutes, take the basket-rack assembly out of the liquid and give it a gentle water rinse. Any enteric coated tablet that clearly displays signs of disintegration fails the test Figure 14. Now swap out the simulated stomach fluid with simulated intestinal fluid in the jar [26] Table 7.

Figure14: Disintegration Apparatus.

Evaluation Parameter	Formulations (Min.)				
	F1	F2	F3	F4	F5
Disintegration Test	9	17	11	14	15

Table 7: Disintegration time.

Dissolution Test

Drug release was assessed using equipment II to conduct an enteric coated tablet disintegration test in accordance with IP using method B. This approach utilised two distinct pH levels at two separate time periods. The tablets were submerged in 900 mL of 0.1 N hydrochloric acid in the USP dissolving bath for the first stage (pH 1.2), which was carried out at a temperature of 37 0.5o C. The 50 rpm paddle stirring speed was chosen. The device was filled with six tablets, and it was run for two hours. Following the procedure described above, a fluid sample was taken and evaluated for the presence of DFS discharged. The acid phase must not have more than 10% DFS dissolved, according to the standard. The vessel was then emptied of acid, and pH 6.8 phosphate buffer was added. This final buffer was made by combining 0.20 M tribasic sodium phosphate (3:1) with 0.1 M hydrochloric acid.

At various times throughout this buffer phase, sample aliquots were taken out and the amount of DFS dissolved was measured. The buffer phase must dissolve at least 80% of the medication after 90 minutes. The samples were analysed using the HPLC technique at a wavelength of 254 nm [27]

Table 8 and Table 9.

Evaluation Parameter	Formulations (min.)				
	F1	F2	F3	F4	F5
Dissolution Test	62	54	52	48	65

Table 8: Dissolution Test.

S. No.	Evaluation Parameters	Values	Marketed Tablet
1	Hardness of Tablet(kg/cm^2)	4 kg/cm^2	4kg/cm^2
2	Friability Test (≥1%)	0.20%	>1%
3	Thickness of Tablet	5.58mm	3.5mm
4	Dieameter of Tablet	10.08mm	8-10 mm
5	Dissolution Test	65 Min.	1hr.
6	Disintegration Time	15 min.	15 min.
7	Average weight in mg (within the limit ±5%)	469mg	200-400 mg

Tablet 9: Tablet Comparison with Marketed Product.

Conclusion

To sum up, making enteric-coated diclofenac sodium tablets is a challenging procedure that demands close attention to detail and adherence to precise instructions. The pills' ability to withstand the stomach's acidic environment and transfer the drug to the small intestine, where it may be efficiently absorbed, is due to the employment of specialized coating processes. The resultant delayed release formulation has demonstrated efficacy in lowering fever, discomfort, and inflammation while lowering the possibility of gastrointestinal adverse effects. The creation and improvement of enteric-coated diclofenac sodium tablets is a big step forward in the treatment of a variety of inflammatory disorders and can greatly enhance patient outcomes. Additional investigation is required to fully investigate this formulation's potential and to discover explore the full potential of this formulation and to identify other potential applications in clinical practice.

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