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Physical Assessment and formulation development of Dome Matrix Controlled Release tablet of Diclofenac Sodium

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Abstract

In the last fifteen years where have significant acceleration in drug delivery research. In the early days of controlled release, development of pharmaceutical formulations was more idealized, with emphasis on the attainment of the illusive "zero-order release behavior". When analyzing the swelling and release behavior of the Dome Matrix systems, it was demonstrated that the swelling behavior of the curved surfaces of the matrices strongly affected the drug release kinetics. The controlled release Dome matrix tablets containing Diclofenac sodium were prepared using a wet granulation process and polymers used xanthan gum, HPMC and Eudragit. Two different formulations were prepared; in first formulation the ratio was kept 60% active ingredient and 40% polymers subsequently in 2nd formulation 55% active ingredient 45% polymers. Precompression test angle of repose, Hausner's ratio, Bulk Density, Tapped Density, Car's Index were checked according to the specified standard procedure. All Physical Characteristics of dome tablets were analyzed. Drug release pattern was also analyzed by using USP apparatus II paddle method. The hardness, weight fluctuation, thickness, friability, drug content homogeneity, and in-vitro dissolution investigations of the manufactured controlled release tablets. All were examined and found within acceptable range. The F1 and F2 formulations performed well in tests and had a continuous drug release. The findings of this study showed that a polymer could be successfully used to formulate Diclofenac sodium Dome matrix tablets. The drug release was extended for 8 to 12 hours in all formulations using a drug to polymer ratio of 60:40, 55:45. The formulations are proved to have efficient drug release time.

Keywords: Diclofenac sodium, Dome Matrix, Eudragit, Control release, Xanthan gum.

INTRODUCTION

In the last fifteen years there has been a significant acceleration in drug delivery research. In the early days of controlled release, development of pharmaceutical formulations was more idealized, with emphasis on the attainment of the illusive "zero-order release behavior". Recently, research has returned to a more realistic approach for solution of pharmaceutical application problems. Thus, development of new pharmaceutical formulations is based on classical pharmaceutical technology (e.g., tablets, capsules, powders, FDA approved excipients), appropriately designed for the achievement of prolonged release (typically up to 24 h) with controlled, but not necessarily constant release rates [1].

Formulations which might be capable of manipulate the discharge of drug have turn out to be a fundamental part of the pharmaceutical enterprise. mainly oral drug delivery has been the point of interest of pharmaceutical research for many years. This kind of drug shipping has been on the center of research due to its many benefits over conventional dosage. the focal point of this assessment is on matrix capsules because of their broadly use and ease of the system[2].

Modified or controlled release oral drug shipping structures have, over the last few a long time, been shown to offer advantages over conventional structures [3]. those consist of improved patient compliance [4], selective pharmacological motion; decreased aspect-impact profile and decreased dosing frequency [5]. these structures might also therefore have a notably useful results in healing efficacy. managed release offers prolonged transport of medication and upkeep of plasma degrees inside a healing variety[6].

Drug delivery has become an integral feature of novel therapeutic formulations. Drug delivery systems (DDS) allow the release of the necessary drug amount to the correct site and with the desirable kinetics. Most oral drug delivery systems on the market are swell able or swelling matrices, i.e., monolithic systems triggered by the process of water transport in the polymer and the associated drug transport outwards. Swell able matrices respond in the presence of water or biological fluids by changing dimensions and volume by water uptake, allowing the drug to diffuse out of the dosage form. The main component of the swell able matrix is a hydrophilic polymer, initially in its glassy state. When this matrix is in contact with the biological fluid, swelling occurs due to an abrupt change from a glassy to a rubbery state. The person polymer chains, at the start in the unperturbed country, soak up water so that their stop-to-give up distance and radius of gyration expand inside the new solvated nation. that is because of the decreasing of the everyday glass transition temperature of the polymer, determined by means of the swelling agent feature attention and depending on temperature and thermodynamic interactions of the polymer/solvent system [7].

When analyzing the swelling and release behavior of the Dome Matrix systems, it was demonstrated that the swelling behavior of the curved surfaces of the matrices strongly

affected the drug release kinetics. Indeed, the drug release from the convex base is faster and more linear than from the concave base. For further microscopic and molecular analysis, it is desirable to measure the dynamics of swelling evolution and, in particular, the front movement of this curved geometry that cannot be examined with the optical techniques previously used with the flat base matrix [8].

MATERIAL AND METHODS

Equipment's

UV/VI'S spectrophotometer, Tableting machine, HPLC, Dissolution apparatus, Vernier caliper, Disintegration apparatus, Friabilator, Hardness tester, USP 26 Apparatus, Hydroxypropyl methylcellulose (Premium Methocel K100M), Ultrasound equipment, Eudragit S 100, Xanthan Gum, Mg state and Acetone

Pre-formulation Studies

Standard Diclofenac Sodium Graph

The standard curve of Diclofenac Sodium were drawn according to the standard procedure by using 100 mg of Diclofenac sodium in 100 ml solvent (pH 6.7). This solution was further kept for 30 minutes complete dissolution and different dilutions made as per standard procedures.

Precompression.

The pre-formulation studies will be conducted according to standard method as prescribed which comprised of angle of repose, Hausner's ratio, Bulk Density, Tapped Density, Carr's Index according to the specified standard procedure

Procedure

Formulation Development

The active ingredient was kneaded in a motor and pestle and after kneaded this powder was pored through science no 125 and then mixed with polymers and ingredient. Two different formulations were prepared, in first formulation the ratio was kept 60% active ingredient and 40% polymers subsequently in 2nd formulation 55% active ingredient 45% polymers. All the ingredients were mixed thoroughly for 15 minutes than with the help of tableting machine Magnesium striate in acetone was used to lubricate the punches of the tableting machine to keep them from sticking.. The punches were shaped differently in four different shapes that was cylindrically flat base matrices, The second cylindrical matrix has a flat base, the third one has a convex base, and the fourth matrix has a concave base.

Physical Characteristics of dome tablet

Weight Variation Test

Weight variation for tablets have been randomly selected and weighed individually with the help of an analytical stability. The average weights were determined and the proportion deviations from imply values had been calculated. The proportion weight version for each tablet was anticipated in keeping with the following formulation:

% Weight variation = (common Weight-individual Weight) / character Weight × 100

Surface area measurement

Surface area of the dome tablets were performed according to the specification of all formulation.

Drug Release Parameter

By using USP apparatus II paddle method. The rotation will be kept 75rpm and the temperature will be kept 75% and the medium will be filled upto 900ml. the samples will be collected accordingly to the different time intervals.

Mathematical Interpretation

For evaluation of the percentage release of dissolution compared with the standard were calculated by statistical formula.

A= a.b.ceq. 1

Fraction release = $\frac{m}{m}\infty = \frac{V}{m\infty}$. A/a.b.c eq. II

Hardness Test

Hardness Test was determined by using "Monsanto" type hardness tester. The mean crushing strengths (hardness values) were determined.

Friability Test

For friability test, drugs were randomly selected, weighed and located into the Friabilator chamber set at 25 rpm for 1 minute. The capsules had been weighed once more and the variations in weight have been calculated as the percentage friability.

Dissolution

Dissolution studies were performed according to USP monographs or standards. The basket rotation was kept 100/ rounds per minute and temperature maintained accordingly at 37 ± 0.1 ^{0}C. Than the sample (5ml) were collected at time intervals specified, after that the samples were be examined by the help of UV- Visible Spectrophotometer.

RESULTS

Standard Diclofenac Sodium Graph

The standard graph of Diclofenac Sodium (Table 1) displays strong linearity, with R2 values of 0.1856 and 0. 0.1968 in 0.2 NHCl (Fig. 1) and pH 6.7 buffer (Fig. 2), under a maximum of 295 nm, demonstrating that it abides by Lambert's "Beer-law."

Table 1: Standard Diclofenac Sodium Graph

Conc. (mcg/ml)	Absorbance at 295nm	
	0.1 NHCl	6.7 pH Buffer
5.	0.149	0.145
10.	0.218	0.238
15.	0.328	0.362
20.	0.438	0.443
25.	0.412	0.555
30.	0.505	0.661
35.	0.618	0.779
40.	0.760	0.848
45.	0.732	0.944
50.	1.309	1.021
R^2	0.1856	0.1968

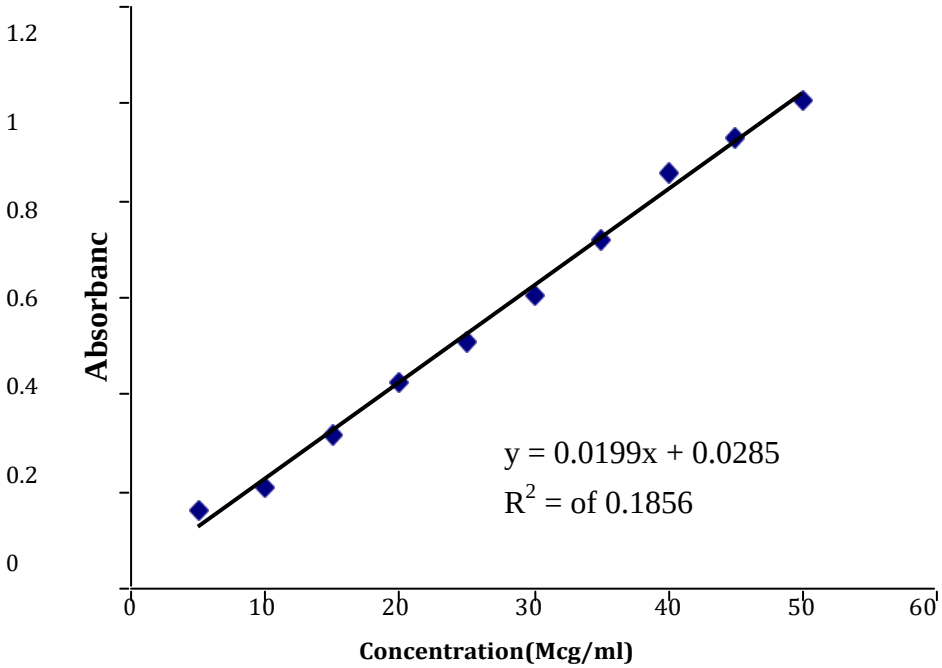


Figure 1: Diclofenac Sodium Standard Graph in 0.1 NHCl

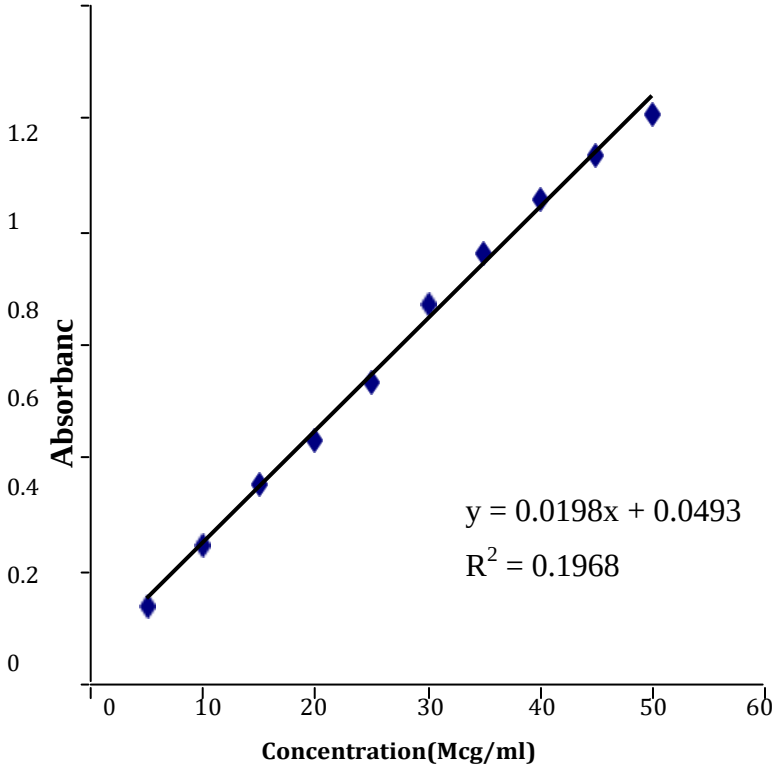


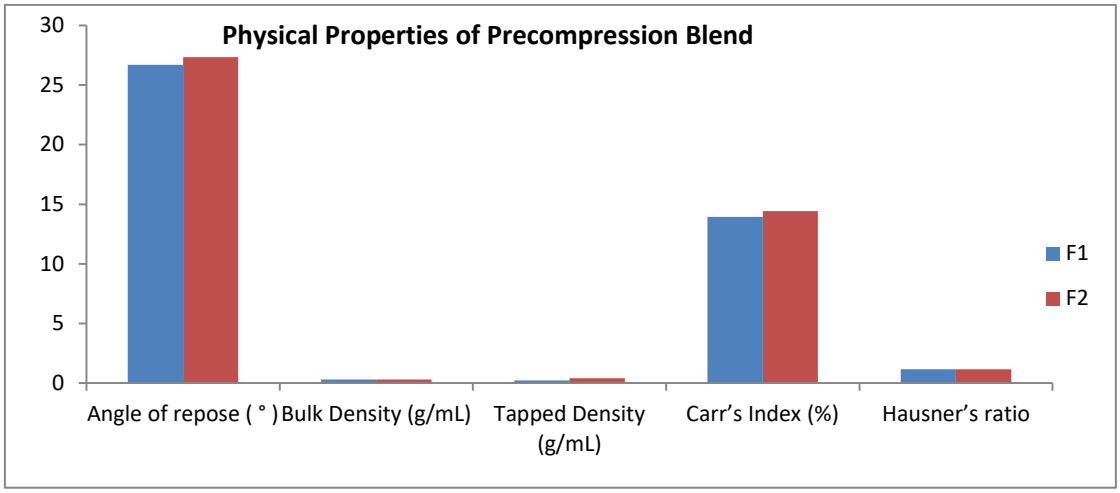
Figure 2. Diclofenac Sodium Standard Graph in 6.7 pH Buffer

Granule Characterization

The Carr's index, bulk density, tapped density, drug content, and attitude of repose were used to characterise the matrix pill granules. Angle of repose decreased to less than 35 degrees, and Carr's index values for all batches of granules were less than 21, suggesting genuine flow ability and compressibility. For all of the batches, Hausner's ratio was substantially lower than 1.25, indicating proper flow homes. In excess of 90% of all the granules of various formulations' medication content.

Table 3: Physical Properties of Precompression Blend:

Formulations	Angle of repose (°)	Bulk Density (g/ml)	Tapped Density (g/ml)	Carr's Index (%)	Hausner's ratio
F1	26.70	0.311	0.231	13.94	1.16
F2	27.34	0.305	0.410	14.43	1.17



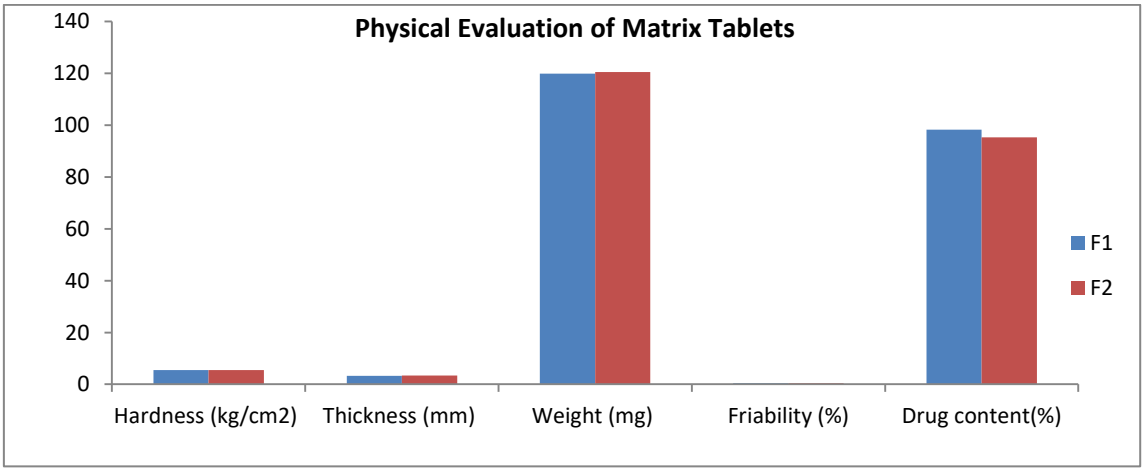
5.4 Matrix tablet physical evaluation:

Table Four provides the effects of the matrix tablets' consistency of weight, hardness, thickness, friability, and medication content. Due to the fact their weights various among 119.nine and 120.5 mg, all the capsules from unique batches met the legitimate requirements for weight uniformity. The matrix drugs' hardness numerous from 5.50 to 5. Forty-five kg/cm, and their friability become much less than zero.38 percentage, displaying that they had been compact and difficult. The medicinal drugs' thickness ranged from three.22 to a few.37 mm. all the formulations met the medication's content material requirements, containing 95 to 99 percentage Diclofenac Sodium and precise drug homogeneity. cloth becomes discovered. as a result, all the bodily attributes of the organized capsules were located be nearly inside control.

Table 4: Physical Matrix tablets' evaluation

F.Code	Hardness (kg/cm²) †	Thickness (mm) ‡	Weight (mg) ‡	Friability (%)	Drug content * (%)
F1	5.49 ±0.54	3.56±0.18	126.9±1.44	0.37	95.89±1.39
F2	5.45±0.41	3.07±1.27	131.5±0.52	0.38	99.76±0.79

All of the values cited in above desk taken mean ± well-known Deviation (SD), n=three
† All the values noted in above table taken mean ± general Deviation (SD), n=6
‡ All the values stated in above table taken suggest ± popular Deviation (SD), n=20

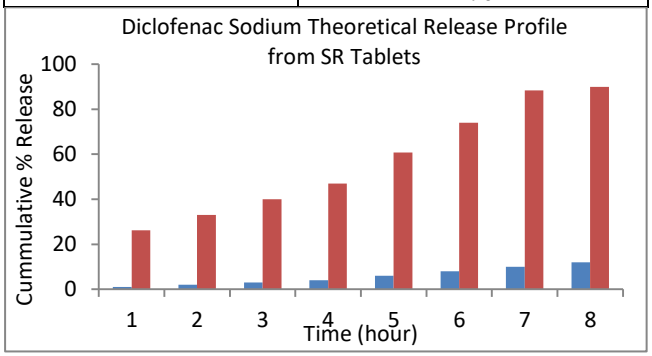


Theoretical Release Profile and Dose Calculations

The dose that was calculated early than the necessary full dose for two times-day by day maintain release system of Diclofenac Sodium changed into found to be a 100 mg as well as its theoretical release profile is stated in Table2.

Table 2: Theoretical Release Profile of Diclofenac Sodium from SR tablets

Time (hours)	Cumulative % Release
1	25.15
2	32.18
3	39.99
4	45.98
6	61.01
8	73.90
10	87.19
12	> 90



DISCUSSION

One of the most cuttingedge sectors of controlled drug deliver y is oral medicine distribution such dosage forms offer a considerable benefit in terms of patient adherence At least a twofold reduction in dosing frequency is achieved with the extended release dosage form. When compared to the medicine delivered in an immediaterel ease (conventional) dose form. Diclofenac sodium is an analgesic and anti-inflammatory medication. It is primarily utilized in the treatment of surgical inflammation and acute painIt is a member of the class of painkillers known as non-steroidal anti-inflammatory medicines (NSAIDs). Inflammation is frequently treated with it, discomfort, acute gout, and ankylosing spondylitis, particularly in low back pain. For this reason, a therapeutic concentration of 100mg/day is required. The therapeutic dose must be maintained for at least 24 hours. Because typical doses release the full medication in a matter of minutes Therapeutic levels are only sustained for a brief period of time. requiring the administration of a second dose as a result, a Diclofenac Sodium sustained release formulation that releases the medicine over a 22-hour period is advantageous.

The goal of this research is to develop and test Diclofenac Sodium extended-release Dome matrix tablets. To improve the release, polymers such as 48 mg Xanthan Gum and 54 mg Eudragit S100 were used to make the controlled release matrix tablet.

CONCLUSION

The goal of this study was to prepare Diclofenac sodium-controlled release Dome matrix tablet formulation that would keep therapeutic levels of the drug constant for more than 12 hours. These types of formulation would be safer and continuous release which ultimately benefits the community in response to diseases.

The controlled release Dome matrix tablets containing Diclofenac sodium are made using a wet granulation process and various grades of polymers Xanthan gum, HPMC and Eudragit.

Diclofenac Sodium is an analgesic remedy. As a result, an attempt become made to hold the therapeutic awareness regular for an extended time. This was achieved with the aid of growing a drug shipping machine with a regulated launch. these managed launch Dome matrix tablets had been in most cases designed to launch the drug for an extended time, i.e., 12 hours, and to absolutely launch the drug at the same time as fending off excessive dosage periodicity. The hardness, weight fluctuation, thickness, friability, drug content homogeneity, and in-vitro dissolution investigations of both formulations were within the acceptable range and the released rates were near 90% in 12 hours. The findings of this study showed that a polymer could be successfully used to formulate Diclofenac sodium control release Dome matrix tablets. The drug release mechanism of these formulations were checked and compared with other formulations, it was found that all these formulations were extended for 8 to 12 hours with different drug to polymer ratio of 60:40, 55:45. The formulations are proved to increased release time. As a result, it can be stated that Diclofenac sodium in the form of a once-daily controlled release matrix tablet has a reasonable extended-release profile, suggesting that it may improve therapeutic efficacy. The drawbacks and restrictions of extended-release medications are overcome and removed by the new formulation.

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