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Research Article

Formulation and characterization of Aceclofenac dispersible tablet

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Abstract

The aim of this study was to formulate and characterization of dispersible tablet (Aceclofenac). Aceclofenac is a phenylacetic acid belongs to the group of non-steroidal anti-inflammatory drug (NSAID). It causes by inhibition of COX-2 and prostaglandin E2(PGE2) synthesis in blood mononuclear and polymorphonuclear cells.It used as anti-rheumatic, anti-inflammatory (both acute and chronic),analgesic (effective pain killer in lower backache, dental or gynecological pain) and antipyretic. In present study, disintegrants(crospovidone and sodium starch glycolate) with are used. Evaluation of different batches of tablets by thickness, weigh variation, hardness, friability, drug content uniformity, wetting time, water absorption ratio, *in-vitro* disintegration time and *in-vitro* drug release. Quantitative analyzes of aceclofenac by UV-Spectrophotometry, High Performance Liqud Chromatography (HPLC) and Mass Spectroscopy. Three formulation patterns were used for *in-vitro* drug release study.

Keywords-Aceclofenac, crospovidone, sodium starch glycolate, *in-vitro* disintegration time

Introduction

Oral administration is the most important route of any drug delivery to the systemic circulation (Shukla et al., 2017).Novel drug delivery systems (NDDS) aim to formulating a dosage form of drug molecules for convenient management and to achieve better patient compliance.

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To obviate the problems associated with conventional dosage forms, orally fast disintegrating tablets have been developed, which combine hardness, dosage uniformity, stability and other parameters, with extremely easy administration, since no water is required for swallowing the tablets and they are thus suitable for geriatric, pediatric and traveling patients.Aceclofenac [[2-(2', 6'-dichlorophenyl) amino] phenylacetoxyacetic acid] is a phenylacetic acid belongs to the group of non-steroidal anti-inflammatory drug (NSAID). It is a pro-drug ofdiclofenac and decomposed under hydrolytic stress (neutral, acidic, and alkaline) and also on exposureto light (in solution form).It causes preferential inhibition of COX-2 and prostaglandin E2 (PGE2) synthesis in Blood mononuclear and

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polymorphonuclear cells. Aceclofenac had no effect on interleukin-8 production (Kuchekar etal., 2001, Wikman et al., 1993, Welling et al., 1984)).

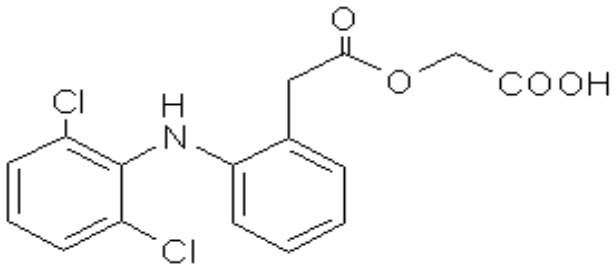

Figure1. STRUCTURE OF ACECLOFENAC

In the present work, the oral dispersible tablets of aceclofenac were prepared by two different super disintegrants crospovidone and sodium starchglycolate. aceclofenac was estimated by UV-visible spectrophotometeric method (Shimadzu - 1700) in different dissolution fluids.Evaluation of different batches of tablets by thickness, weigh variation, hardness, friability, drug content uniformity, wetting time, water absorption ratio, *in-vitro* disintegration time and *in-vitro* drug release.

MATERIALS AND METHODS

Aceclofenac was obtained from G. D. Lab. Pvt.Ltd., New Delhi. Crospovidone and sodium starch glycolate were obtained from Signet Chemicals Pvt. Ltd., Mumbai. All other chemicals of analytical grade were purchased from commercial sources.

METHODOLOGY

1. PREPARATION OF DISPERSIBLE TABLETS

Tablets were compressed directly from the mixture of the drug and excipients without any preliminary treatment**.** The mixture to be compressed must have adequate flow properties and cohere under pressure thus making pre-treatment as wet granulation unnecessary**.**Dispersible tablet of Aceclofenac was formulated using 2 % and 4 % of disintegrants Crospovidone, Sodium starch glycolate, Guar gum and Ispaghula by conventional dry granulation.The wet screening process involves converting the moist mass into coarse, granular aggregates of passing through screen (sieve-22). This material was compressed using Cadmach single punch tablet machine.After compression tablets were heated in a hot air oven at 60°C the complete removal of volatilizable component (Lachman et al., 1987, Bos et al., 1991)).

2. PREFORMULATION STUDIES

2.1. Solubility of Aceclofenac

Solubility of aceclofenac was tested in various media. Different types of media were prepared and taken for UV absorbance of the solutions after appropriate dilutions were determined at 273 nm. Phosphate buffer at pH7 were show the highest solubility. Results were shown in figure2.

2.2. Determination of λ_{max} for Analysis

Solutions of aceclofenac were prepared in the different dissolution medium and organic solvents. λ_{max} was determined by scanning between 200-400 nm, using spectrophotometer.Results were shown in figure3.

2.3. IR Spectroscopy

Drug pellets of 0**.**1mm were taken and grind it with potassium Bromide in pressure compression machine. The sample was mounted in IR compartment and scanned at wavelength 4000 cm^{-1} – 500 cm^{-1}. The results were shown in figure4.

2.4. Calibration Curve

2.4.1. Calibration Curve of Aceclofenac in purified water

Aceclofenac tablets were dissolved in methanol and diluted with purified water**.** Absorbance was estimated by UV-visible spectrophotometer at 274 nm. Calibration curve were shown in figure5.

2.4.2Calibration Curve of Aceclofenac in HCl pH 1.2

Prepared stock solutions were taken and diluted it with HCL**.** Absorbance was estimated by UV-visible spectrophotometer at 274 nm. Calibration curve were shown in figure6.

2.4.3. Calibration Curve of Aceclofenac in phosphate buffer of pH 7.0

Prepared stock solutions were taken and diluted it with phosphate buffer**.** Absorbance was estimated by UV-visible spectrophotometer at 274 nm. Calibration curve were shown in figure7.

3. EVALUATION OF DISPERSIBLE TABLET

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3.1 Evaluation of Blends

Flow properties of granules were determined by angle of repose method. Compressibility index of granules were determine by Carr's index and Hauser ratio.

3.2Evaluation of Dispersible Tablet

3.2.1 Thickness

Thicknesses of table were measured by Vernier Caliper. From the formulation twenty tablets were picking up randomly and take for thickness measurement.

3.2.2 Weight Variation

Digital electronic balance is used for weight variation. Twenty tablets were selected randomly from a batch and average weight was determined.

3.2.3 Hardness

Hardness of tablet relates both disintegration and drug dissolution. Hardness of tablet was determined using Pfizer tester. The tablet was compressed between a holding ansil and a piston connected to a direct force reading gauge.

3.2.4 Friability

Friability of the tablets was determined using Roche friabilator. This tool subjects that tablet to the combine effect of abrasions and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inch in each revolution. Pre-weighed twenty tablets were placed in the friabilator, which is then operated for 100 revolutions.

3.2.5 *In vitro* dispersion time

In vitro dispersion time was calculated by dropping a tablet in a measuring cylinder containing 6 ml of water. Three tablets from each formulation were randomly selected and *in vitro* dispersion time was performed (Chakraborty et al., 2008).

3.2.6 *In vitro* dissolution studies

For *In vitro* dissolution studies, drug was carried out using USP paddle method at 75 rpm in 900 ml of phosphate buffer pH 7.0 as dissolution media, maintained at 37° ± 0.5. Aliquots were withdrawn at each specified time intervals filtered through whatmann filter paper and assayed spectorphotometrically at 274 nm. The *in vitro* permeation data obtained were subjected to a zero order and first order kinetics.

RESULTS AND DISCUSSION

Aceclofenac were prepared by using disintegrants(Crospovidone and Sodium starch glycolate). Wet granulation and dry granulation is used for preparation of aceclofenac tablets. The hardness of these tablets was found to be 2.5 to 5.8 kg/cm^2, determined by the Pfizer hardness tester. All tablets have friability less than 1 %. Disintegration time of the tablets was determined by disintegration tine apparatus using distilled water as the disintegration medium at 25 ± 1°. All tablets were disintegrated within 15 s to 120 s.The flow properties of the powder mixture are important for the uniformity of mass of the tablets; the flow of the powder mixture was analyzed before compression to tablets. Different Calibration curve are made at different pH.The important parameter that needs to be optimized in the development of disintegrating tablets is thedisintegration time of tablets.*In vitro*dispersion time was performed and results were shown in figure 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 19.

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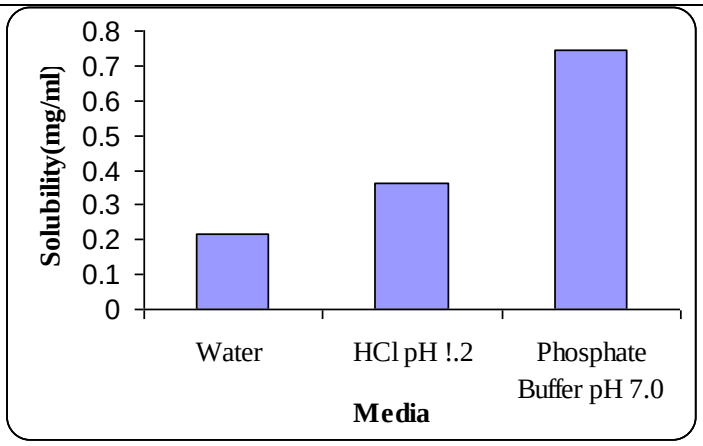

Figure2. Solubility of Aceclofenac in Different Media

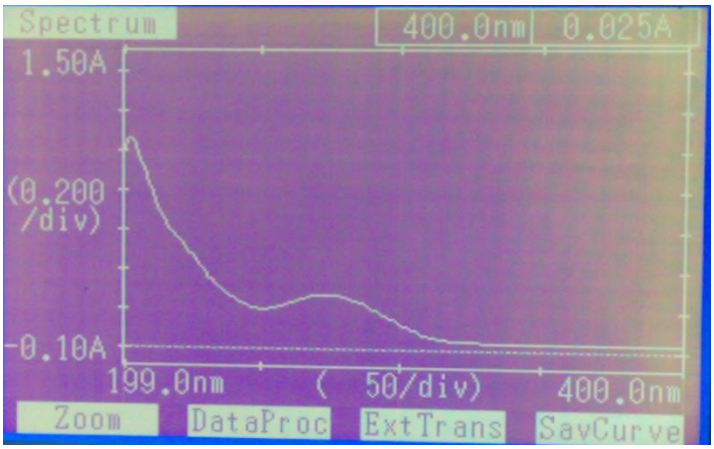

Figure3.λ_{max} (nm) of Aceclofenac

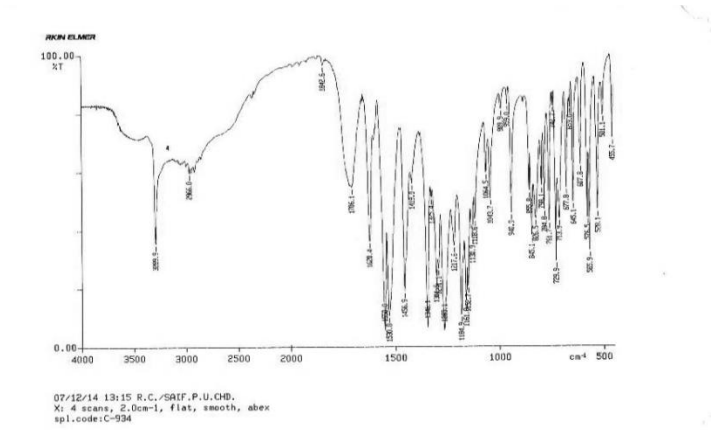

Figure4. IR of Aceclofenac

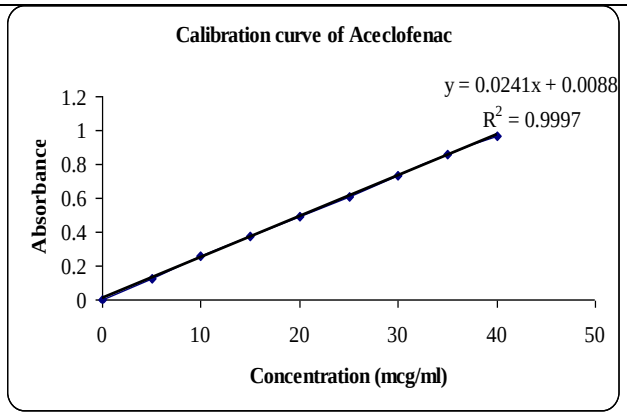

Figure5. Calibration Curve of Aceclofenac in Purified Water

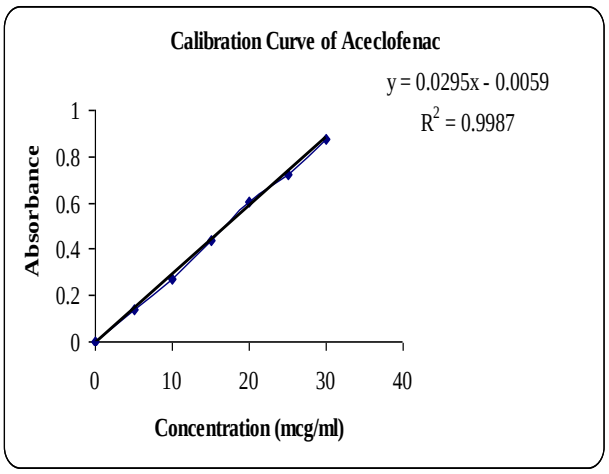

Figure6. Calibration Curve of Aceclofenac in HCl pH 1.2

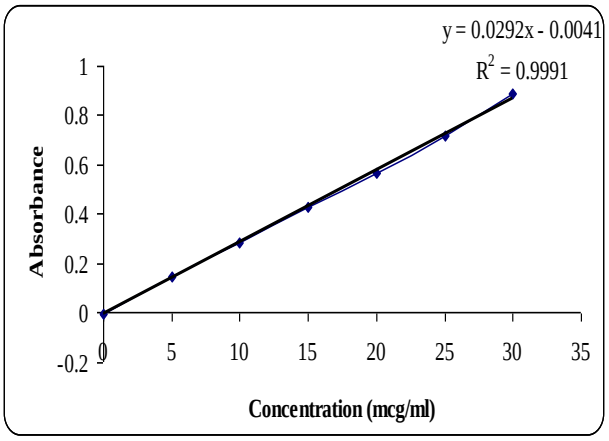

Figure7. Calibration Curve of Acecofenac in Phosphate Buffer pH 7.0

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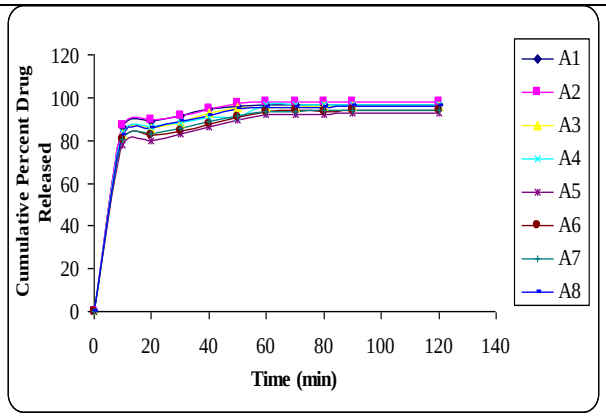

Figure8.*In Vitro* Drug Release of Aceclofenac Tablet by using Direct Compression Method (Zero Order Release)

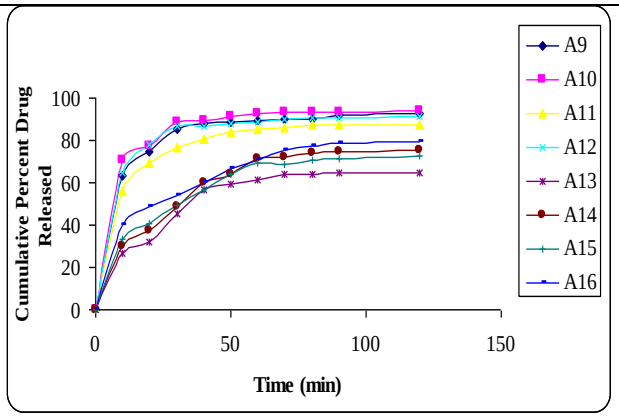

Figure11.*In Vitro* Drug Release of Aceclofenac Tablet by using Dry Granulation Method (Zero Order Release)

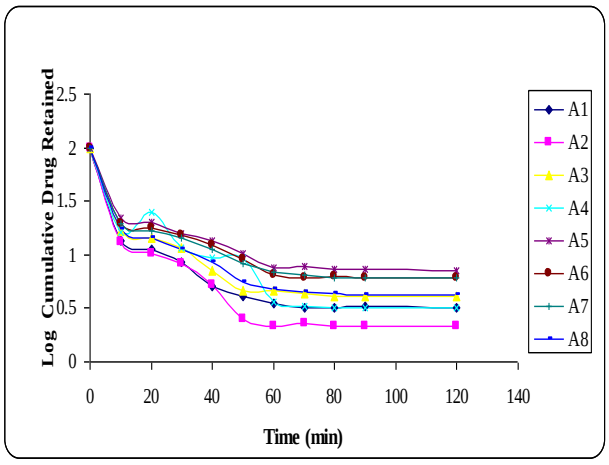

Figure9. *In Vitro* Drug Release of Aceclofenac Tablet by using Direct Compression Method (First Order Release)

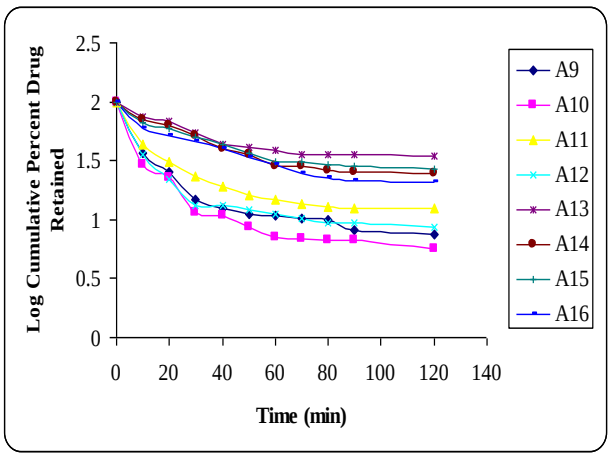

Figure12. *In Vitro* Drug Release of Aceclofenac Tablet by using Dry Granulation Method (First Order Release)

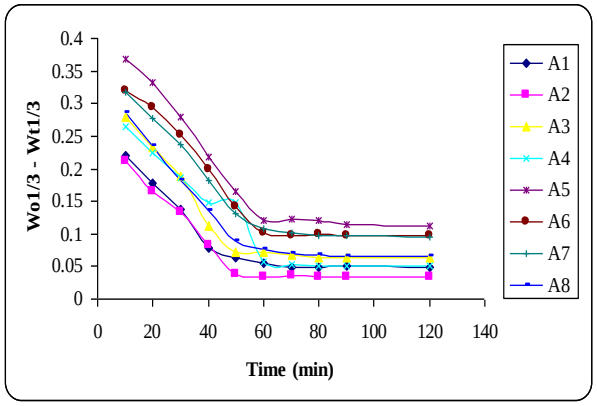

Figure10.*In Vitro* Drug Release of Aceclofenac Tablet by using Direct Compression Method (Hixon-Crowell Cube Root Model)

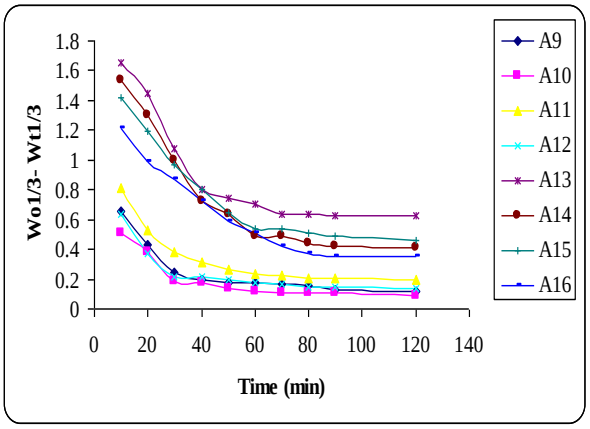

Figure13.*In Vitro* Drug Release of Aceclofenac Tablet by using Dry Granulation Method (Hixon-Crowell Cube Root Model)

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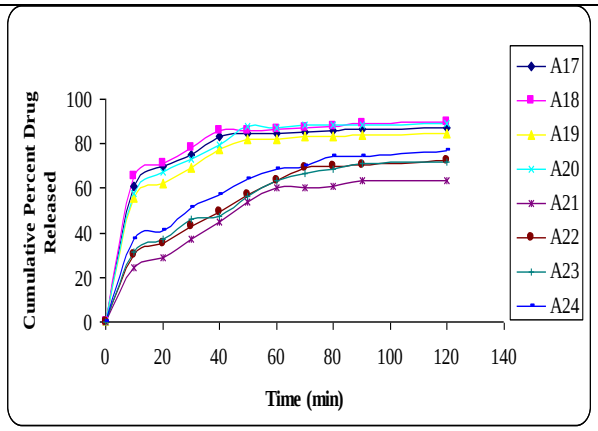

Figure14. *In Vitro* Drug Release of Aceclofenac Tablet by using Wet Granulation Method (Zero Order Release)

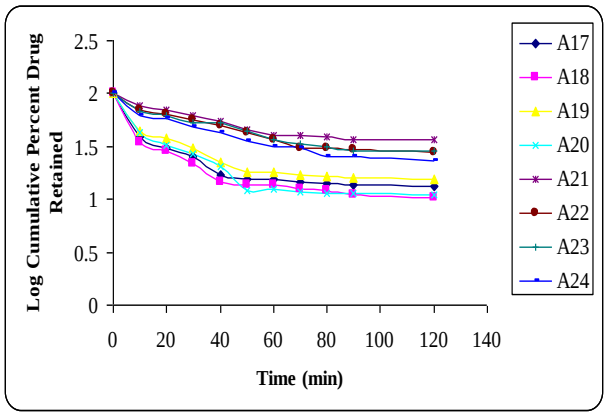

Figure15.*In Vitro* Drug Release of Aceclofenac Tablet by using Wet Granulation Method (First Order Release)

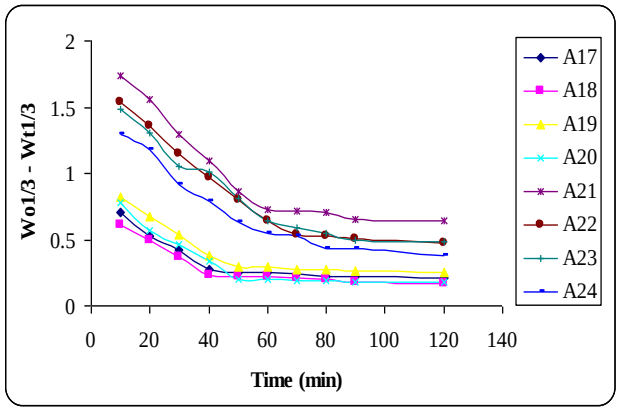

Figure16. *In Vitro* Drug Release Data of Aceclofenac Tablet by using Wet Granulation Method (Hixon-Crowell Cube Root Model)

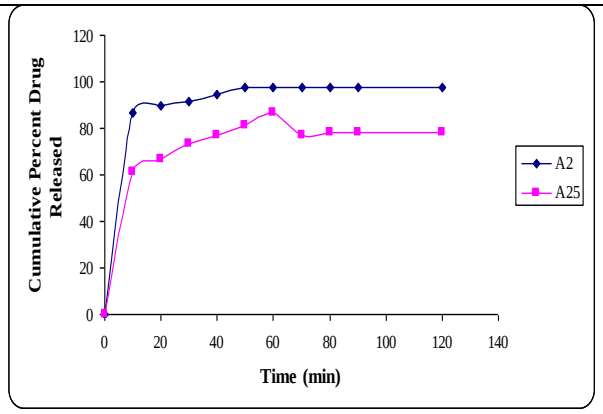

Figure17. Comparison of *in Vitro* Drug Release of Prepared Tablet of Aceclofenac with Marketed Formulation (Zero Order Release)

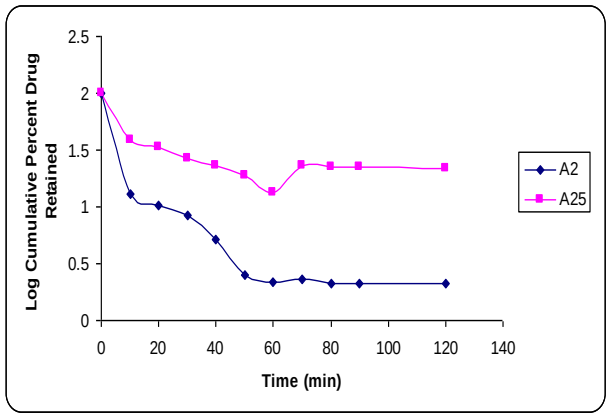

Figure18. Comparison of *in vitro* Drug Release of Prepared Tablet of Aceclofenac with Marketed Formulation (First order release)

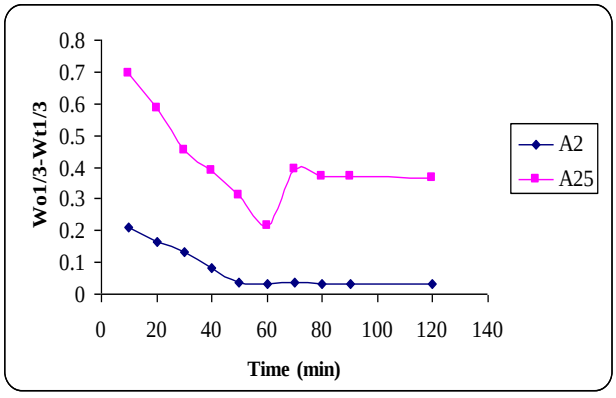

Figure19. Comparison of *in Vitro* Drug Release Data of Prepared Tablet of Aceclofenac with Marketed Formulation (Hixon-Crowell cube root model)

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SUMMARY AND CONCLUSION

The objective of present study was to formulate and evaluate dispersible tablets of aceclofenac using natural and synthetic disintegrants. The objective of present study was to formulate and evaluate dispersible tablets of aceclofenac using natural and synthetic disintegrants. Geriatric and pediatric patients have trouble in swallowing conventional tablets, which leads to poor patient compliance. To overcome this weakness, we have developed innovative drug delivery system known as "fast dispersible tablet"or "rapidly disintegrating tablet". Aceclofenac inhibits cyclo-oxygenase enzyme and prevents the production of prostaglandins from arachidonic acid. It reduces joint inflammation, pain intensity and duration of morning stiffness in patients with rheumatoid arthritis. Its biological half-life 4.3 h is very short and therefore is an ideal candidate for rapid release drug delivery system. Formulation of aceclofenac dispersible tablet is not presently available so aceclofenac was selected as drug candidate to formulate dispersible tablet. The sample of aceclofenac was tested for their purity by Infra-Red Absorption (Shimadzu-460). Melting point, chemical test and other test were performed for the purity of the drug sample as drug is included in standard monographs. Aceclofenac drug was also analyzed by solubility, partition coefficient and maxima wavelength. All these disintegrants were used in 2-4 % concentration in the dispersible tablets and formulated twenty-four formulations of the drug. Formulation was evaluated for friability, weight variation, thickness and dissolution studies of the formulated products were performed using USP XXII Dissolution Test Apparatus. The drug contents of aceclofenac in dispersible tablet were found to be which determined by UV-spectrophotometer at 274 nm respectively. The hardness of these tablets was found to be 2.5 to 5.8 kg/cm^2, determined by the Pfizer hardness tester. All tablets have friability less than 1 %. Disintegration time of the tablets was determined by disintegration tine apparatus using distilled water as the disintegration medium at 25 ± 1°. All tablets were disintegrated within 15 s to 120 s. Weight variation was determined by the digital electronic balance. Dispersion pattern of the tablets were estimated using

50 ml of distilled water at 25 ± 1° using two tablets in the container and samples was stirred for proper dispersion of the tablets. It was passed through mesh no. 22. Dissolution studies were performed using USP XXII Dissolution Test Apparatus (paddle assembly) at 75 rpm using 900 ml of phosphate buffer (pH 7.0) at 37° ± 0.5 throughout the studies of all formulations. 5 ml of samples were withdrawn at a regular interval of time and replaced with fresh phosphate buffer and drug contents were determined using the UV- spectrophotometer. Dissolution parameters followed Hixson-Crowell cube root equation. Dissolution as well as disintegration time were compared with the marketed conventional tablets of aceclofenac. Hence, it was concluded that direct compression method was found to be more effective in the preparation of aceclofenac dispersible tablets. From this study it is possible to design suitable dispersible tablet containing aceclofenac for the treatment of inflammation with more effectiveness and better patient compliance. Futher *in-vivo* investigations are required to correlate *in-vitro* drug release studies for the development of suitable rapid release system of aceclofenac.

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