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Formulation and Evaluation of Aceclofenac Solid Dispersion for Improving the Solubility and Dissolution Rate

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Abstract: *Aceclofenac is a novel non-steroidal anti-inflammatory drug (NSAID) having anti-inflammatory and analgesic properties. It is widely used in the treatment of rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis. One of the major problems with this drug is its low solubility in biological fluids, which results into poor bioavailability after oral administration. For overcoming this problem, we have designed a research work to formulate solid dispersions (SDs) of Aceclofenac which was prepared using Kneading method with the carrier PEG, urea and guar gum to increase its aqueous solubility. Aceclofenac SDs were prepared in 1:1, 1:3 and 1:5 ratios of the drug to polymer. Physicochemical evaluation was performed such as p^H study, dissolution study, solubility study. In-vitro release profiles of all formulations (F-1 to F-9) were comparatively evaluated and also studied against pure aceclofenac and visual inspection. The concentration of diffused drug was measured using UV-visible spectrophotometer at λ_{max}= 276 nm. Among the carriers faster dissolution was exhibited by the formulations of SD containing urea than PEG and Guar gum. The experimental results show that the solid dispersion of Aceclofenac has improved dissolution rate and the formulated system shows good bioavailability in a short time. Highest solubility percentage (42.25%) was found for F-8; and F-7 showed highest dissolution rate in 60 minute (87.92%). The increase tendency of dissolution rate of the drug may be due to increase in wettability, hydrophilic nature of the carrier and due to reduction in drug crystallinity. However, further investigation is required to establish in-vivo and in-vitro correlation to confirm the accurate pattern of drug release from Aceclofenac SDs for potential therapeutic use.*

Keywords: *Aceclofenac, Solid dispersions (SDs), Dissolution study, Solubility study.*

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I. Introduction

Aceclofenac (ACF) is a non steroidal anti inflammatory cytokine inhibitor which is broadly used for the symptomatic treatment of pain and inflammation specifically in rheumatoid arthritis, osteoarthritis and ankylosing spondylitis with the recommended dose of 100 mg twice daily **[1].** The drug works by inhibiting the action of cyclooxygenase (COX) that is involved in the production of prostaglandins (PG) which is accountable for pain, swelling, inflammation and fever **[2].** Aceclofenac ($C_{16}H_{13}C_{l2}NO_4$), chemically [2-{2,(6-dichlorophenyl) amino}] phenylacetooxyacetic acid], is a crystalline powder with a molecular weight of 354.19 and it is practically insoluble in water with good permeability **[3].** It is metabolized in human hepatocytes and human microsomes to form [2-(2',6'-dichloro-4'-hydroxy-phenylamino) phenyl] acetoxyacetic acid as the major metabolite, which is then further conjugated **[4].** Aceclofenac falls under the BCS Class II, poorly soluble and highly permeable drugs **[5].** So, dissolution rate limited absorption is shown by ACF that gives rise to difficulties in pharmaceutical formulations for oral delivery, which may lead to under medication or overmedication as the steady state concentration values fall or rise beyond the therapeutic range **[6].** Some factors that affect the amount of drug available for its effect (the bioavailability of the drug) other than solubility and permeability are dissolution rate of the drug, first-pass effect, pre-systemic metabolism of the drug in any other organ, and susceptibility to efflux mechanisms. Solubility of the drug in the gastric media is a major problem with most drugs **[7].** At least 40% of the new chemical molecules tested are drugs having poor aqueous solubility. Many methods are available to improve dissolution rate, solubility characteristics, including salt formation, micronization, and addition of solvent or surface active agents. Solid dispersion is one of these methods, which was most widely and successfully applied to improve the solubility, dissolution rates and consequently the bioavailability of poorly soluble drugs. Sekiguchi and Obi *et al.* first significantly enhanced rate and extent of sulfathiazole absorption using the solid dispersion technique **[8]**. The main objective of this work was to investigate the possibility of improving the solubility and dissolution rate of Aceclofenac by

preparing SD with various water-soluble polymers such as PEG, guar gum and urea. The prepared SD was evaluated for solubility study, drug content, *in-vitro* dissolution rate studies.

II. Materials And Methods

2.1 Materials and equipment:

Aceclofenac (potency 95.5%), Methanol, pH meter (HANNA instrument), UV-Vis spectrophotometer (UV-1700, Shimadzu, Japan). All other chemicals and apparatus were analytical grade and supplied from the laboratory of Dept. of Pharmacy, NSTU, Bangladesh.

2.2 Methodology

Weighed quantity of carrier was placed into a mortar moistened with water and kneaded to the paste consistency. Then weighed quantity of drug was introduced slowly and kneaded for 30 min. During this process appropriate quantity of water was added to maintain suitable consistency. Finally, the obtained paste was dried in at water bath at 40 °C until the water was removed completely and stored in desiccators over fused calcium chloride after sieving with 60 mesh size sieve. Nine formulations have been prepared by using kneading method which is shown in Table 1.

Table 1. Formulations of the Aceclofenac Solid Dispersions

Formulation No.	Composition	Drug: Polmer
F-1	Aceclofenac + PEG	1: 1
F-2	Aceclofenac + PEG	1: 3
F-3	Aceclofenac + PEG	1: 5
F-4	Aceclofenac + Urea	1: 1
F-5	Aceclofenac + Urea	1: 3
F-6	Aceclofenac + Urea	1: 5
F-7	Aceclofenac + Guar gum	1: 1
F-8	Aceclofenac + Guar gum	1: 3
F-9	Aceclofenac + Guar gum	1: 5

2.2.1 Maximum wavelength absorption determination

Samples were filtered and then assayed by UV-Vis spectrophotometer (UV-1700, Shimadzu, Japan) at 273 nm. To determine the concentration of sample, we used standard curve prepared by using pure active drug.

2.2.2 pH study

pH study has been also done successfully. pH test of the formulation is performed in distilled water. pH was determined for each formulation using a pH meter (HANNA instrument).

2.2.4 Solubility study

Phase solubility study was carried out in order in to ascertain effect of carriers on the solubility characteristics of aceclofenac. Solubility of aceclofenac SDs were evaluated for observing the improvement of the solubility.

2.2.4 Dissolution study

Dissolution of aceclofenac from various dispersion methods were studied in 900 ml in water at 37 ± 0.50ºC using USP dissolution test apparatus-II employing paddle stirrer at 100 rpm for 60 minute. A sample of dispersion formulation mixture equivalent to a 1g of aceclofenac was used in each test. At predetermined time intervals, 5 ml of the sample was withdrawn using a syringe fitted with a prefilter and simultaneously replacing with fresh 5 ml dissolution fluid. These collected samples were analyzed for aceclofenac (from SDs) content by measuring the absorbance at 276 nm.

III. Results

3.1 Visual assessment of the formulated SDs

We found different formulation show different colors. For the formulations **F1**: opaque; **F2**: transparent; **F3**: transparent; **F4**: opaque; **F5**: opaque; **F6**: slightly opaque; **F7**: totally opaque; **F8**: opaque; **F9**: slightly opaque.

3.2. Results of pH study

The pH data for solid dispersion showed that there are variations among pH of the different formulations (Table 2).

Table 2. pH values of the different formulated SDs

Formulation	pH of Solid Dispersion
F1	6.18
F2	6.88
F3	6.43
F4	6.32
F5	6.33
F6	6.39
F7	6.04
F8	6.26
F9	6.40

3.3 Results of solubility study

Aceclofenac is practically insoluble in water. To improve its solubility, we try to prepare solid dispersions. Solubility studies with different solvents or combination of solvents (water and methanol) were performed. The solubility test result is shown in Table 3 and the increment of solubility due to formulating the SDs is given in Figure 1.

Table 3. Solubility testing data for the solid dispersions

Formulation	% of drug release in Water (y)	% of SD release using Water (x)	% of SD release using Water: Methanol = 50:50	% of SD release SD using Methanol
F1	9.21	28.43	67.2	96.11
F2	11.25	35.62	62.46	98.34
F3	8.13	39.27	73.94	93.23
F4	5.5	32.76	65.15	87.20
F5	8.98	28.23	62.12	90.15
F6	12.45	35.55	54.84	98.11
F7	4.61	28.92	52.88	92.13
F8	9.76	42.26	68.75	91.10
F9	12.65	40.65	65.68	90.50

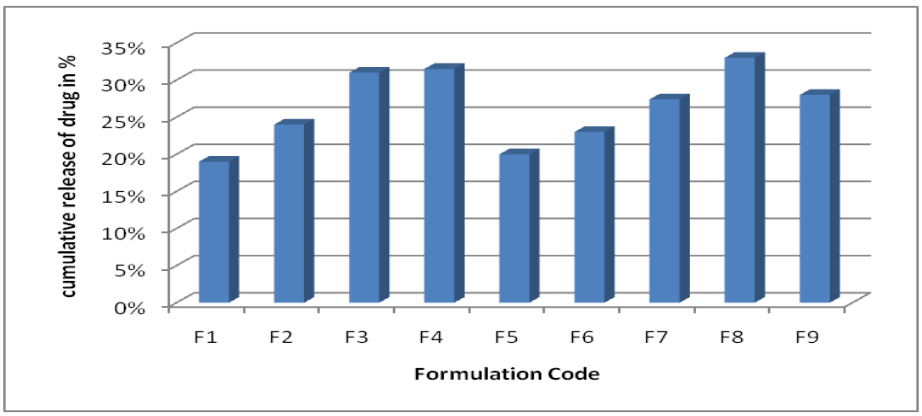

Figure 1. Diagram of % of solubility increased by preparing solid dispersion

3.4 Results of dissolution study

In-vitro dissolution profiles of the different SDs were shown in Figure 2. We found that SDs containing guar gum has highest dissolution profile after 1hr.

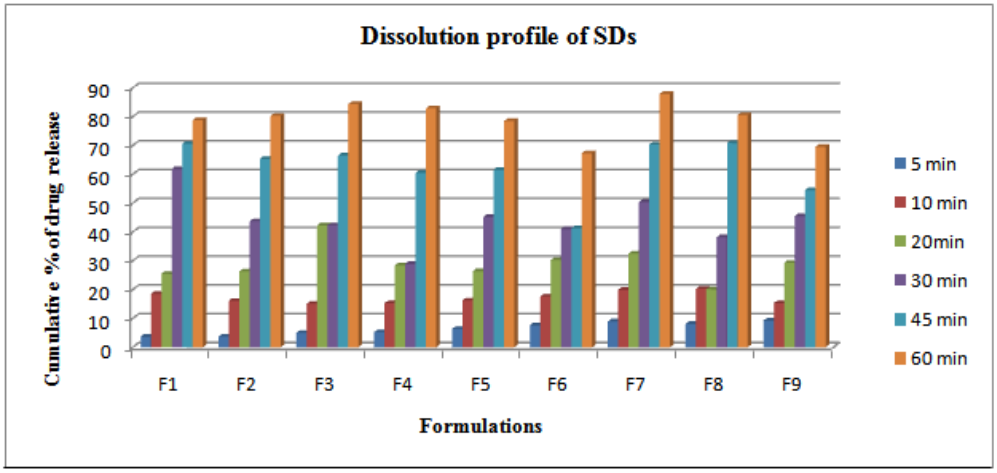

Figure 2. Dissolution profile of solid dispersions.

IV. Discussion

From the above pH data we can observe that all of the results are slightly above the pH 6. Solid dispersed formulation F1 has shown the pH 6.18. Then for F2 and F3, pH values are 6.88 and 6.43 respectively. pH of F4 fall slightly amounting 6.32; whereas for F5 and F6, they were 6.33 and 6.39 respectively. Then F7 decrease the pH in 6.04, which again increase in F8 6.26 and in F9 6.40. pH in our intestine gradually changes from pH 6 to pH 7.4. So we can easily conclude that our formulations will also absorb from the intestine rather than stomach **[10].** Solubility testing information about SDs helps to overcome the solubility problem with drug solubility. % of pure drug release in water is 9.21 which increased in formulation F1 28.92% in water. Solubility increased more in solvent water: methanol 50:50. 67.20% which is further increased in full methanol 96.11%. Drug release % is 11.25, when F2 release 35.62% in water. Then next time drug release % decrease that 8.13 than previous release but F3 increase much higher that is 39.27. F4 release 32.76% but pure drug release in so much lower rate 5.5%. F5 release 28.23% but drug release 8.98%. F6 release 35.55% where drug release 12.45%. But in this time F7 release rate decrease abruptly than F6 that is and drug release 4.61%.F8 release 28.92% where drug release 9.76%. F8 release 42.26% where drug release 9.76%. At last F9 release 40.65% and drug release 12.65%. So it is clear from the above data that F8 release is high than all of the formulation 42.26% than pure drug 9.76%. The F8 formulation carrier was guar gum. So guar gum has the higher soluble capability than urea and PEG. The dissolution study shows that formulation F1 show 3.63% drug release in first 5 minute but it increase in next 10 minute but little increase in 20 minute which is significantly change in 30 minute. Again in 45 minute it has lower increment which is higher in 60 minute 78.81%. In 5 minute formulation F2-F9 there is no moderately change. In case of F2 dissolution rate was 3.72% then in 10 minute dissolution rate was 16.08% in 20, 30, 45 minute the dissolution increase consecutively which was higher in 60 minute & dissolution rate was 80.25%. In 5 minute F3 dissolution rate was 4.96% which is little increase in 10 minute but in 20 and 30 minute there is steady state change which is higher in 45 and 60 minute. Formulation F4 dissolution rate was 5.25% in 5 minute but there was no noticeable change next 10, 20 and in 30 minutes but higher dissolution rate was in 60 minute 82.90%. In case of F5 there was also consecutive change which is also higher in 60 minute 78.5%. Again F6 dissolution rate was 7.6% in 5 minute in 10 and 20 minute there is comparatively increment but in 30 and 45 minute there is steady state change but high in 60 minute 67.28% which is lower than previous 60 minute release data. In F7 there is also consecutive change but in 60 minute the dissolution rate is higher than all other formulation 87.92% it is the highest release data. In F8 dissolution rate is 8.12% in 10 and 20 minute there is steady state change which is high in 60 minute 80.52%. Last formulation F9 dissolution rate was 9.27% in 5 minute in 10 minute there is little increment in 20 minute there is also increment in 30, 45 and 60 minute there is again consecutive change. In 60 minute dissolution rate is 69.54% which in not higher than previous 60 minute release rate. So now it is clear that formulation F7 has the highest dissolution rate in 60 minute (87.92%) and the carrier was guar gum. So guar gum has the comparatively higher capability than urea and PEG.

V. Conclusion

Our study reveals that, all the chemical parameters for ideal solid dispersion were satisfactory for the manufacturing process. We found that preparing solid dispersion of Aceclofenac significantly increase the solubility and dissolution profile of the drug. The data generated from this experiment showed that preparing the SDs using guar gum strongly improve the dissolution rate than using PEG and Urea. However, further

investigation is required to establish In-vivo and In-vitro correlation to confirm the accurate pattern of drug release from SDs for potential therapeutic use.

References

[1]. Ahmed T, Ferdous A, Biswas SK, Sharif F. Assessments of Dissolution Profile of Aceclofenac Tablets Available in Bangladesh. S. J Pharm Sci. 2010; 3(1):1-3.
[2]. Raza K, Kumar M, Kumar P, Malik R, Sharma G, Kaur M, Katare O.P. Topical Delivery of Aceclofenac: Challenges and Promises of Novel Drug Delivery Systems. Biomed Res. Int. 2014; 2014:1-11.
[3]. Islam SMA, Islam S, Shahriar M, Dewan I. Comparative in vitro dissolution study of Aceclofenac Marketed Tablets in Two Different Dissolution Media by Validated Analytical Method. J Appl Pharm Sci. 2011; 1(9):87-92.
[4]. Yu LX, Amidon GL, Polli JE, Zhao H, Mehta MU, Conner DP et al. Biopharmaceutics classification system: the scientific basis for biowaiver extensions. Pharm. Res. 2002; 19(7):921-925.
[5]. Drug Profiles: Aceclofenac. Institute of Pharmaceutical Sciences and Research Center, Bhagwant University, 2016.
[6]. Banker GS, Anderson NR. The Theory and Practice of Industrial Pharmacy. Edn 3, Lea & Febiger Verghese publishing house, Philadelphia, 1986, 293-303.
[7]. Savjani KT, Gajjar AK, Savjani JK. Drug Solubility:Importance and Enhancement Techniques. ISRN Pharm.2012; 2012: 1-10.
[8]. Keiji S, Noboru O. Studies on absorption of eutectic mixture. I.A comparison of the behavior of eutectic mixture of sulfathiazole an that of ordinary sulfathiazole in man. Chem Pharm Bull.196; 9(11): 866-872.
[9]. Bano R, Gauhar S, Naqvi SBS, Mahmood S. Pharmaceutical evaluation of different brands of Levofloxacin tablets (250 mg) available in local market of Karachi (Pakistan). Int. J Curr Pharm Res. 2011; 3(1):15-22.
[10]. Amidon GL, Lennernas H, Shah VP, Crison JR. A Theoretical Basis for a Biopharmaceutic Drug Classification: The Correlation of In Vitro Drug Product Dissolution and in Vivo Bioavailability. Pharm Res.1995; 12(3):413-420.

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