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Formulation and *in vitro* evaluation of Aceclofenac effervescent tablets

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Abstract
Aceclofenac, a non steroidal anti-inflammatory drug (NSAID), inhibits the enzyme cyclooxygenase which is responsible for the production of prostaglandins. It is the glycolic acid ester of diclofenac. The present work is based in designing effervescent tablets of aceclofenac.
The aceclofenac effervescent tablets were prepared by wet granulation method. The alterations in the effervescence time of the prepared tablets were studied by varying the concentrations of acid and base materials, i.e. citic acid, sodium bicarbonate and tartaric acid. On the basis of the effervescence time, an optimum formulation was chosen.
The results revealed that the formulated batch which consists of 20% w/w, 50.85% w/w and 25.58%w/w of citric acid, sodium bicarbonate and tartaric acid respectively was chosen as an optimum formulation with effervescence time of 276.5 seconds. And as we increase or decrease the amount of citric acid and sodium bicarbonate from the amount used for the optimum formulation, the effervescent time tend to increase as observed in formulations. So the concentrations of the citric acid and sodium bicarbonate must be as that of F8 (optimum formulation) to get the better effervescent time. Therefore, aceclofenac effervescent tablets can be prepared by wet granulation method.

Keywords: *Aceclofenac, effervescence time, citric acid, tartaric acid, sodium bicarbonate*

1. Introduction
Studies have demonstrated that effervescent tablets and powders enhance absorption of a number of active ingredients (e.g. disulfiram and caffeine), compared to conventional formulations. That's because the carbon dioxide created by the effervescent reaction can induce enhanced active-ingredient permeability due to an alteration of the paracellular pathway. The paracellular pathway is the primary route of absorption for hydrophilic active ingredients in which solutes diffuse into the intercellular space between epithelial cells. It is theorized that the carbon dioxide alters (widens) the intercellular space between cells, which leads to greater absorption of active ingredients (both hydrophobic and hydrophilic). The increased absorption of hydrophobic active ingredients could be due to the non-polar carbon dioxide gas molecules partition into the cell membrane, thus creating an increased hydrophobic environment, which would allow the hydrophobic active ingredients to be absorbed [1].
Other major advantages of effervescent aceclofenac tablets are as follows:

- A palatable liquid dosage form is provided as an alternative to the solid form.
- An effervescent formulation is useful for patients who need or prefer to take a liquid formulation, particularly elderly patients and those with dysphagia.
- Since a liquid formulation is more palatable than solid dosage form, it is more acceptable to patients and results in greater adherence to the prescribed therapy regimen.
- A liquid containing the effervescent formulation provides an immediate and sustained increase in intragastric pH. The effervescent mixture also provides an immediate transient increase in pH of the esophagus and stomach. This buffering action provides immediate relief, yet there is no rebound in acid secretion because ranitidine blocks the H_2 -receptors. This property is especially useful in dyspepsia and NSAID induced gastritis.
- An effervescent formulation provides the stability of a dry formulation, yet is easily convertible into liquid form [2, 3].

Therefore, the main objective was to formulate and evaluate effervescent aceclofenac tablets.

2. Materials and Methods

2.1. Materials

Aceclofenac was obtained as gift sample from Lomus Pharmaceuticals Pvt. Ltd. Citric acid, tartaric acid, sodium bicarbonate, PVP-K-30 and Magnesium stearate were used as excipients. All reagents and other chemicals were of analytical grade and obtained from our laboratory.

2.2. Methods

The tablets were formulated and compressed by wet granulation method. The formulations were prepared first by sieving all the excipients through sieve no. 60 and the active ingredient aceclofenac was sieved through sieve no. 16. Pvpk 30 was added to a small amount of isopropyl alcohol and mixed to form a binding solution. Citric acid, tartaric acid, sodium bicarbonate and aceclofenac were mixed thoroughly by using spatula. Then the previously prepared binding solution was added to the mixture and again mixed properly. Then, the wet mass was spread and kept in a hot air oven for certain time. After drying for certain time, the mixture was passed through a sieve to form granules of suitable size. After the preparation of granules, the granules were mixed with a measured amount of magnesium stearate, lubricating agent, in a plastic bag and finally compressed using 16mm die and punch.

The tablets were characterized for general appearance, thickness, weight variation, hardness, friability and effervescence time [4, 5]. For determination of λmax, weighed amount of aceclofenac was dissolved in methanol to obtain a 1000mcg/mL solution. This solution was subjected to scanning between 200 – 400 nm and absorbance maximum was determined. The effect of dilution on absorption maxima was studied by diluting the above solution to 20mcg/mL and scanned from 200 – 400nm [5].

2.3. Preparation of standard calibration curve in methanol

A stock solution of standard aceclofenac of 100µg/ml concentration was prepared in methanol. The stock solution was then used to prepare the standard working solution of five different concentration 10, 15, 20, 25, 30 µg/ml respectively. The absorbance of each sample solution was measured at λmax using methanol as a blank.

2.4. Assay

Twenty tablets from each batch were weighed and pulverized in a mortar. The samples of powder equivalent to average weight were taken and transferred to a 50ml volumetric flask. The powder was then dissolved in a methanol for 20 minutes. The solution was then filtered through Whatman no.1 filter paper and the filtrate was suitably diluted to produce final solution of 20µg/ml concentrations. The absorbance of the resulting solution was measured at λmax. The process was repeated thrice and corresponding three readings were recorded. Mean value of three concentrations with standard deviation was calculated [5, 6].

3. Results and Discussion

The spectrum of 20mcg/ml solution of aceclofenac was prepared and scanned in UV visible spectrophotometer. The solution gave absorbance maxima at 275nm.

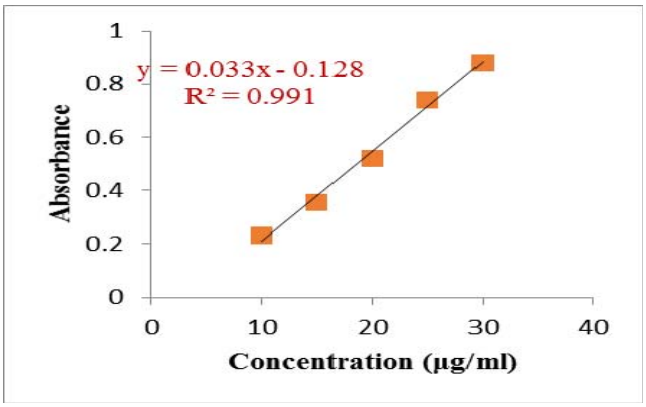

Fig. 1: Calibration curve of Aceclofenac in methanol

The calibration curve for different concentration Aceclofenac RS versus absorbance was plotted. It was shown in above Figure 1. The correlation coefficient for Aceclofenac in methanol was found to be 0.9917. It showed that there was good correlation between concentration and absorbance at that range.

Fourteen formulations of batch size100 were prepared by wet granulation. The composition of all the formulations is shown in Table 1.

Table 1: Composition of various formulations

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14
Aceclofenac (mg)	100	100	100	100	100	100	100	100	100	100	100	100	100	100
Citric Acid (mg)	401.25	300	225	225	375	300	375	300	375	375	450	450	525	525
Sodium bicarbonate (mg)	852.9	852.7	852.7	927.7	927.7	927.7	762.7	762.7	687.7	612.74	612.74	537.7	537.7	462.7
PVP – K 30 (mg)	30.75	30.75	30.75	30.75	30.75	30.75	30.75	30.75	30.75	30.75	30.75	30.75	30.75	30.75
Tartaric acid(mg)	207.3	308.7	383.7	308.7	158.7	233.7	308.7	383.7	383.7	458.7	383.7	458.6	383.7	470.6
Magnesium stearate (mg)	7.8	7.8	7.8	7.8	7.8	7.8	7.8	7.8	7.8	7.8	7.8	7.8	7.8	7.8
Total mg	1600	1600	1600	1600	1600	1600	1600	1600	1600	1600	1600	1600	1600	1600

The tablets were 16 mm flat faced bevel edged, white in color, round and uncoated with few small visible pores and slight chipping. The physicochemical parameters was tested [7]. and assay of tablets are as shown in Table 2:

Table 2: Physicochemical Parameters and Assay

Formulation	Weight ariation Mean (n=10;mg)	Thickness Mean (n=5;mm)	Hardness Mean (n=2; kg/cm^2)	Effervescent time (n=2 ;sec)	Lag time (n=6 ;sec)	Assay (n=10 ;%)
F1	1602.2	5.372	4.3	543	139	92.61
F2	1599.3	5.193	4.1	468	121	97.72
F3	1598.2	4.79	4.4	623	84	102.37
F4	1599.1	4.616	4.3	549.5	107	90.11
F5	1603.5	4.988	4.4	470	125	105.23
F6	1598.7	5.15	4.4	945.5	79	110.34
F7	1608.2	5.404	4.3	342.5	61	105.13
F8	1605.3	5.85	4.2	276.5	57	97.62
F9	1600.2	5.772	4.3	386.5	51	96.61
F10	1597.5	5.312	4.2	673	118	95.12
F11	1604.1	6.056	4.4	471.5	135	97.62
F12	1598.3	4.9	4.3	502.5	126	104.23
F13	1603.2	5.546	4.2	321	41	95.32
F14	1596.55	5.31	4.2	357	59	101.1

As shown, the thickness of the tablets varied from 4.616mm to 6.056 mm. The weight of the tablets varied from 1596.55 mg to 1608.2 mg. The friability of all the formulations was found to be less than 1%.

The hardness of the tablets varied from 4.1 kg/cm2 to 4.4 kg/cm2. The assay of the tablets varied from 90.11% to 110.34%. The effervescence time of the tablets varied from 276.5 s to 945.5 s. The effervescence time of different formulations with varying concentrations of acid and base was compared, upon comparison F8 showed the lowest effervescence time and F6 showed the highest effervescence time. The formulated batch F8 contains 20% w/w, 50.85% w/w and 25.58%w/w of citric acid, sodium bicarbonate and tartaric acid respectively while F6 contains 300 mg (20%w/w), 927 mg (57.93%), and 383 mg (23.93%) of citric acid, sodium bicarbonate and tartaric acid respectively. It showed that increase in concentration of tartaric acid greatly reduces the effervescence time but reduces the incidence of picking and sticking during the process of tablet compression. Decrease in effervescence time on reducing concentration of sodium bicarbonate from highest concentration in F6 to lower concentration in F8 also suggest that better effervescence time can be obtained with optimal concentration of base forming agent. The concentration of citric acid should also be optimal as it is hygroscopic in nature and increased concentration leads to sticking and picking during tablet compression. Hence, of all the formulations F8 was identified as an optimal formulation on the basis of effervescence time.

4. Conclusion

Different formulations of effervescent aceclofenac tablets were prepared by varying amount of acid source (citric acid anhydrous and tartaric acid) and carbon dioxide source (sodium bicarbonate) to compare the effervescent time. On the basis of effervescence time F8 was found to be the optimum formulation.

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