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RESEARCH ARTICLE

Preparation and Evaluation of Diclofenac Sodium Effervescent Tablet

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ABSTRACT:

The oral dosage forms are the most popular way of taking medicine although having some disadvantages like deliberate absorption and thus onset of action is extend. This can be overcome by administrating the drug in a liquid form i.e. effervescent tablet. The research is a formulation of diclofenac sodium as a effervescent tablet by wet granulation method. The bitter taste of the drug are masked by added sweetening agent (lactose, glucose etc.) In the present work we are prepared effervescent tablet in that we are used active drug diclofenac sodium and other active ingredient acid like tartaric acid and base sodium bicarbonate in different concentrations. The formulation of tablet was done by using wet granulation, wet granulation is found to be acceptable method of effervescent tablet formulation. The various pre-formulation studies was performed hardness, weight variation, disintegration, dissolution etc.

KEYWORDS: Effervescent tablet, formulation, evaluation, wet granulation, sodium bicarbonate, tartaric acid.

INTRODUCTION:

A tablet is a pharmaceutical oral dosage form or solid unit dosage form of medicaments. They are prepared either by molding or by direct compression.

Types of Tablet:

These types of tablets are futher classified as follow:

1. Oral tablet (oral administration)
2. Chewable tablets (chewed tablet)
3. Buccal tablets
4. Lozenge tablets
5. Soluble tablets
6. Effervescent tablets
7. Implant tablets
8. Vaginal tablets
9. Enteric tablets (enteric coated)
10. Sustained release tablets
11. Sugar coat tablets (sugar coated)
12. Film coated tablets
13. Layered tablets
14. Press coated tablets

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The oral dosage form are the common way of taking medicine although having some difficulties like slow absorption and thus onset of action is extend. This can be overwhelmed by administrating the drug in liquid dosage form but, many API's have partial level of stability in liquid form. So, Effervescent dosage form of tablets acts as an alternative dosage form. The tablet is added into beaker or glass of water just before administration and the drug solution or dispersal is to be drink instantly. The tablet is rapidly broken away from each other by internal liberation of carbon dioxide (CO2) in water (H2O) due to reaction between tartaric acid and citric acid with alkali metal carbonates or bicarbonates in presence of water.(1,2,3). Effervescent tablet defined as the uncoated tablet in general containing acid and carbonates or hydrogen carbonate which react quickly in the presence of water (H2O) release carbon dioxide(CO2) Or Effervescent tablets known as the evaluation of gas bubbles From a water as a result of chemical reaction (4,5). A commonly used as acid in effervescent tablet is citric acid because of its citrous test bicarbonate is the commonly used base but potassium bicarbonate, sodium carbonate and potassium carbonate are used. This tablet when added in a glass of water produce effervescence so they dissolved quickly in water due to the chemical reaction which takes place between bicarbonate and citric or tartaric acid or combination of both.

Reaction:

$3NaHCO3 + C6H8o7.H2O \rightarrow C6H5Na3O7 + 3CO2 + 3H2O$
Sodium Citric Acid Sodium Carbon Water
Bicarbonate Citrate Dioxide

$2NaHCO3 + C4H6O6 \rightarrow C4H4Na2O6 + 2CO2 + 2H2O$
Sodium Tartaric Sodium. Carbon Water
Bicarbonate Acid Tartarate Dioxide 29

Some products are used for pharmaceuticals that damage the stomach or Those which are susceptible to gastric PH. In addition, the drugs or medicament prescribed commonly in high doses may be used in the form of effervescent tablets.[5,6]

History of diclofenac:
Diclofenac was patent bring 1965 by Ciba – Geigy and come into therapeutic use in the united nation in 1988 its available as sodium (Na) or potassium (K) salt.

Advantages:
- They are improving the taste
- It is rapidly absorbed
- It has great bioavailability than other dosage form
- It does not have need to swallow tablet
- It show good stomach and intestine acceptance. (6)

Disadvantages:
- It has larger in size
- It has forms complex production procedure
- It has required delicate packaging procedure. (7)

Effervescent tablets (ET) are used to for this Reasons:
Fast absorption: It is dissolved rapidly in liquid. Some oral tablet like antacid they require more time to absorb in stomach so this is the great way to take tablet because it gives quick and increased absorption.
- Increase in liquid consumption: These tablets provide both therapeutic values and also enhance liquid uptake. In diarrhoea and in summer, consumption of effervescent tablet with water gives to daily liquid intake
- In case of swallowing problem: It present an alternate for these patients which having problem in case of swallowing.
- Simple handling and measuring into exact doses: Tablets are liquefied quickly and the patients can obtain particular doses.

These tablet along with the active medicament contain other ingredients like sodium bicarbonate (NaHCO3), citric acid and tartaric acid which react in the presence of H2O liberating CO2 producing effervescence leading to breakdown of diclofenac sodium is the salt form of diclofenac,

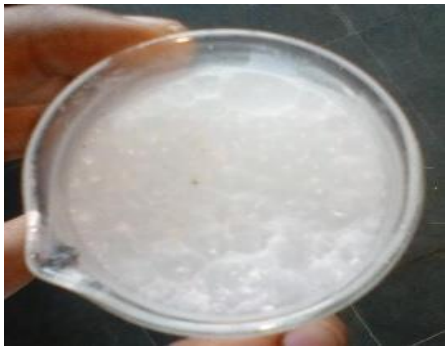


Figure-1: Disintegration of Effervescent tablet

benzene acetic acid derivatives and non- steroidal anti-inflammatory drugs with analgesic (to reduce pain), antipyretic (to treat pyrexia means high body temperature) and anti -inflammatory activity (reduce inflammation which is caused by various causes).[8]

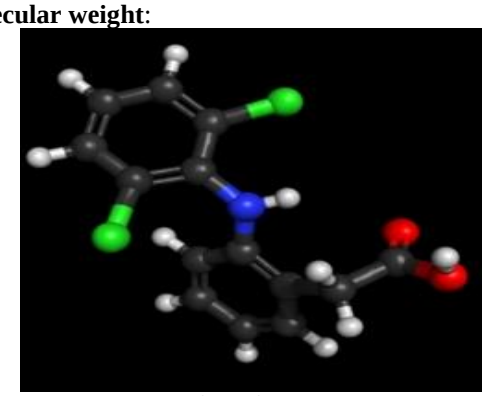
Aim and Objective:-
- The main aim for formulation to despite some disadvantages of medication taking in a oral dosage forms which is most popular ways of taking medication.
- To evaluate prepared effervescent tablets
- To select optimised formulation

Benefits of effervescent tablet over simple tablets:
Easy Alternative to Regular Tablets: They can be a great alternate for those who may have suffering in pain, older individuals or children may have difficulty swallowing but need to take medication or supplements on a regular basis these can be a great way as compared to swallowing of tablets, taking medicine for individuals with various different medical problems that make swallowing difficult and so are a viable alternate to take regular tablets.[6]

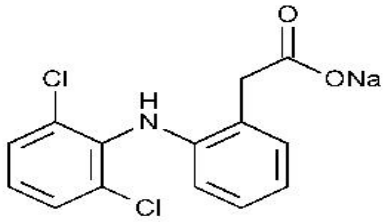
Drug and excipient profile:
Name: Diclofenac sodium

Molecular formula: C14H10CL12NNaO2
Synonyms: Diclofenac sodium, Salt sodium diclofenac etc.

Molecular weight:



Structure-1: **3D Structure of diclofenac**



Structure-2: **Diclofenac sodium**

Mechanism of Action:
The primary mechanism responsible for its anti-inflammatory (reduce inflammation), antipyretic (reduce fever) and analgesic (reduce pain) actions. It's causes inhibition of prostaglandin (PG) synthesis by inhibition of prostaglandin (PG) endoperoxide synthase -2 (PGES-2) also known as cyclo-oxygenase-2 (cox-2). It also exhibits bacteriostatic activity by inhibiting bacterial DNA synthesis.[9,10]

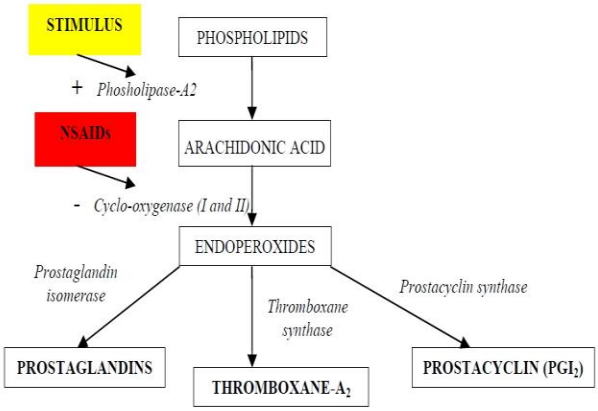


Figure-2: MOA of Diclofenac Sodium (mechanism of action)

Medical uses:
- It is non-steroidal anti-inflammatory drug that exhibit anti-inflammatory (reduce inflammation) analgesic (reduce pain) and antipyretic activities (reduce pyrexia).[11]
- It is also used for treatment of osteoarthritis and Rhumatoid arthritis.[12,13,14]

Material and equipment or Instrument:
Table-1: Material or ingredient

Serial. No.	Material
(1)	Diclofenac sodium(C14H10Cl2NNaO2)
(2)	Sodium bicarbonate
(3)	Tartaric acid
(4)	Propyl alcohol
(5)	Lactose or sucrose
(6)	Mannitol
(7)	Sodium Benzoate or propylene glycol
(8)	Citrous oil

(3,13)

Table-2: **Equipment or instruments**

Serial. No.	Equipment/ Instrument
(1)	Mortar and pestle
(2)	Seive
(3)	Tablet machine
(4)	Monsanto hardness tester
(5)	Pfizer hardness tester
(6)	Frabilator
(7)	Disintegrater
(8)	Dissolution tester apparatus
(9)	Spatula
(10)	Butter paper
(11)	Weighing balance
(12)	Beaker
(13)	Measuring cylinder
(14)	Funnel
(15)	Burette stand
(16)	U.V. Spectroscopy

Method of preparation:
- Diclofenac sodium effervescent tablets are prepared by wet granulation method.

Reaction:

3NaHCO3+ C6H8o7.H2O → C6H5Na3O7 + 3CO2 + 3H2O
Sodium Citric Acid Sodium Carbon Water
Bicarbonate Citrate Dioxide

2NaHCO3 + C4H6O6 → C4H4Na2O6 + 2CO2 + 2H2O
Sodium TartaricAcid Sodium. Carbon Water
Bicarbonate Tartarate Dioxide

Formulation table:

Table-3: Ingredient quantity and uses required for formulation

Sr. No	Ingredients.	Quantity (mg)	Quantity in (gm)	Uses
1	Diclofenac sodium	250	25	Active constituent, NSAID drug
2	Sodium bicarbonate	150	15gm	Antacid
3	Tartaric acid	150	15gm	Acidulent
4	Propyl alcohol	25ml	25ml	Solvent
5	Mannitol	250mg	25gm	Binder
6	Sodium Benzoate or propylene glycol	150ml	15ml	Lubricant
7	Lactose or sucrose	250mg	2.5gm	Sweetning agent
8	Citrous oil	2ml	2ml	Flavouring agent

15,16,17

Procedure:

- In this process, all the materials are weighed accurately mixed in disending direction with each other in a mortal.
- The mixed materials are moistened with a non-aqueous liquid (e.g. alcohol, methyl or propyl alcohol) to form a coherent mass.
- Then this coherent mass transfer through a sieve number 22 or 24.
- After transferring the mass through the sieve and dried the granules in an oven at a temperature not exceeding sixty degree or by air dried.
- Dried granules again passed through the sieve to breakdown the lumps which may formed during drying process
- The granules which is dried are filled in the polyethene bag.

Figure-3: Effervescent Granules

- Then this dried granules are transfer for punching through the punching machine either hand operated or single rotary tablet machine hopper to form a tablet.[18,19]

Figure-4: Effervescent Tablets

Pre-formulation study:

Pre-formulation is termed as a branch of pharmaceutical sciences that develops biopharmaceutical principles The objective of preformulation studies is to select the correct form of the substance, evaluate its physical properties and create through understanding of the material's strength under various circumstances, leading to the optimal drug delivery system. The pre-formulation study emphases on the physiochemical factors that could effect of efficient dosage form. These properties may ultimately afford a the improvement foundation for formulation design. Also it will help in abating problems in later stages of drug development, reducing drug development prices and decreasing products time to market.

OBJECTIVE:

The main object of pre-formulation testing methods is to create information which are beneficial to the formulation in emerging desired, stable and bioavailable dosage form or suitable dosage form.[20]

Pre-formulation is termed as to study of physiochemical properties of the new drug molecule. The aim of pre-formulation studies is to select the correct form of substance.

- Bulk characterisation
- Solubility studies
- Stability analysis

1) Bulk Characteristion:

Evaluation of granules of diclofenac sodium:

1. Bulk density
2. Tapped density
3. Angle of repose
4. Carr's index
5. Hausner's ratio

1) Bulk density:
Bulk density of diclofenac sodium granules was measured by using following formula
Weight of granules = 55.77 gm
Volume of granules = 92
After 100 tapping = 82

Bulk density = weight/bulk volume
= 55.77/92
= 0.60619 g/ml

2) Tapped density:
Tapped density is determined by tapping
Tapped density = weight of granules(gm)/Tap volume
= 55.77/82
= 0.680 g/ml

3) Angle of repose:
Angle of repose were determined by using funnel method.
Angle of repose = R1+R2+R3/3
=11.8+11.6+11.6/3
= 27.26
Theta = tan-1 (h/r)
= tan- 1(2/27.26)
Thete = tan-1(0.00128050)
= 2.234894

4) Carr's index:
Carr's index = Tap density-(Bulk density-tap density/tap density) 100
= (0.606-0.680/0.680)100
= (0.074/0.680)100
= 10.882%

5) Hausners ratio:
Hausners ratio=Tap density/Bulk density (21,22,23)
= 0.680/0.606
= 1.1221 g/ml

2) Solubility:
Solubility of diclofenac sodium are found by used various solvents like water, HCL, NaoH, methyl acetate, benzene, etc. Diclofenac sodium effervescent tablet was soluble in water, NaoH, Hcl more than other solvents.

Table-4: Solubility of diclofenac sodium

Serial No.	Diclofenac Sodium with	Solubility
1)	Ethanol	Poorly soluble
2)	Methyl acetate	Slightly soluble
3)	Benzene	Poorly soluble
4)	Water	Soluble
5)	Hcl	Soluble
6)	NaoH	Soluble

Evaluation parameters:
1) Physical appearance
2) Hardness
3) Friability
4) Disintegration
5) Dissolution

1) Physical appearance:
The general appearance of tablet is visual identification and overall elegance is essential for consumer acceptance for consumer acceptance for control lot to lot uniformity and monitoring trouble free manufacturing.

- **Organoleptic Properties:**

The general organoleptic properties of tablet such as colour, odour, taste are vital means for general evaluation of tablet.

Colour: white
Odour: Odourless
Taste: Bitter

2) Hardness:
Hardness of tablet is the force require to break the tablet in a diametric compression test. Tablet require certain amount of strength or hardness and resistance to mechanical strength during handling, manufacturing, packaging and transportation hardness of tablet are checked by using following hardness tester. (24)
a) Monsanto hardness tester = 0.7 N/mm2
b) Pfizer hardness tester = 0.1 mm N/mm2

3) Friability:
Friability test is performed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and transporting. The instrument is used for this test is known as 'Friability Test Apparatus' or friabilator. Friability test was performed by using frabilator which consists of plastic chamber which is divided into two parts and revolve at a speed 25rpm.

Initial wt. of 10 tablet= 8.4gm
Final weight = 7.88gm
Friability = Initial weight – Final weight
= 8.4-7.88
= 0.52gm

4) Disintegration:
This test is performed to find out that within this test how much time required the tablet disintegrates. This test is necessary for all tablets because the dissolution rate be determined by upon the time of disintegration which ultimately effect the ratio of absorption of drugs. The instruments or apparatus used for this test is called as disintegration method apparatus or disintegrator. The tube is suspended in a bath of water or suitable liquid which is thermostatically maintained at a temperature of 37°C. The tube is allowed to move up and down at a constant rate. Disintegration test were performed time of disintegration are found to be 10 minutes. (25)

Figure-5: Disintegration apparatus

5) Dissolution test:

The rate of dissolution of a solid drug plays an important role in the and physiological availability of the drug in blood stream. Hence determination of dissolution rate of any solid drug is highly important.

Figure-6: Dissolution apparatus

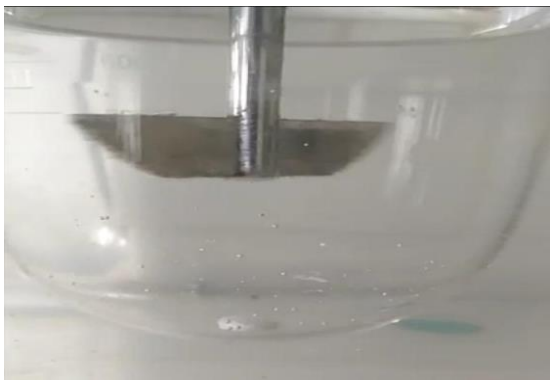


Figure-7: Dissolution of diclofenac sodium tablet

0.2N Hcl are prepared as stated individual monograph is filled glass vessel 0.1N of each bath maintained at 37°C. The tablet is placed in a basket and fitted in position. The motar is started and the revolution is adjusted. The samples are withdrawn at 15, 45, 60, 75, 90 minutes generally 5ml sample solution is withdrawn each time which is replaced with 5ml of medium at 37°C in order maintain at a constant volume in the vessel. (26)

Assay:

Twenty 20 tablets are measured, weighed and powdered in a mortar. The samples equivalent to usual Weight were taken and transported to a 50ml volumetric flask. The powderded sample then solidified in a methanol for 30 minutes. The solution then filtered by using Whatsman filter Paper and the filtrate suitably diluted to yield final Solution of 30µg/ml concentrations. The resultant solution absorbance measured at lamda max (λmax) The process Repeated more times and corresponding three interpretations were Recorded. (27). The sample are tested by UV following results are obtained. In UV spectroscopy set the lambda max of diclofenac sodium two hundred and seventy six 276 nm taken approximately and then following test are performed in photometric mode

Table-5: Absorbance readings after several time intervals

Time (minutes)	Absorbance	K* Absorbance
15	0.8796	584.03
30	0.9067	655.56
45	0.9123	602.96
60	0.9198	598.23
75	0.9211	515.97
90	0.9312	444.15

RESULTS:

- Pre-formulation study:

(1) Bulk characteristion:

(a) Bulk density = 0.60619
(b) Tapped density=0.680
(c) Angle of repose=9.7824
(d) Carr's index =10.33
(e) Hausners ratio= 1.1221

(2) Solubility:

Solubility of diclofenac sodium are found to be More in water, NaoH, Hcl, by using various solvents.

- **Evaluation of preparation**

1. Organoleptic properties:

(a) Colour = White
(b) Odour= Odourless
(c) Taste = bitter

2. Hardness:

a) Monsanto hardness tester: 0.7kg
b) Pfizer hardness tester: 0.1kg

3. Friability: 0.44

4. Disintegration time: 25-30 minutes

5. Dissolution: 30 minutes

CONCLUSION:

- Formulating these effervescent tablets by wet granulation method is better than in dry granulation and direct compression because it serves a good distribution of active ingredient.
- To study managed to improve of diclofenac sodium solution palatability by utilisation of saccharin using effervescent formula.
- These effervescent tablets prepared by using wet granulation method two tablet must provide or give 500 mg of active ingredient (diclofenac sodium) or four tablets give 1000mg.

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