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Formulation and Evaluation of Superdisintegrants on Diclofenac Tablets

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ABSTRACT: The purpose of this research was to mask the intensely bitter taste of Diclofenac sodium and to formulate a rapid - disintegrating tablet.To formulate an orally disintegrating tablet so that it can be administered to paediatric and geriatric patients.Fast disintegrating tablets of Diclofenac sodium containing different concentrations of super disintegrants were prepared by wet compression method all the ingredients without magnesium stearate and talc were sifted through the sieve #44 and are mixed for about 15min to make a uniform blend. Magnesium stearate and talc were passed through sieve #60 and mixed with above powder for sufficient time, usually 5-7mins.
The prepared powder were evaluated for various preformulation parameters like bulk density, tapped density ,angle of repose, carr's index and Haunser ratio and compressed using sixteen station rotary tableting machine. Finally all the evaluation tests were conducted.
KEYWORDS: Super disintegrants, Disintegration, Tablet, diclofenac and dissolution

- **AIM:**

The aim of the present study is to formulate and evaluate fast disintegrating tablets of Diclofenac by wet granulation method employing super disintegrating agents.

OBJECTIVE:

The objective of present study:

- The purpose of this research was to mask the intensely bitter taste of Diclofenac sodium and to formulate a rapid - disintegrating tablet.

- To formulate an orally disintegrating tablet so that it can be administered to paediatric and geriatric patients.

I. INTRODUCTION

1.1 Fast Dissolving Tablets:

United States Food and drug administration (FDA) defined fast dissolving tablet (FDT) as "a solid dosage form containing medicinal substance or active ingredient which disintegrate rapidly usually within a matter of seconds when placed upon the tongue."

FDTs differ from traditional tablets as they are designed to be dissolved on the tongue rather than swallowed whole.

Fast dissolving tablets are also known as mouth-dissolving tablets, melt-in mouth tablets, Orodispersible tablets, porous tablets, quick dissolving tablets, fast dissolving tablets.

According to US Food and Drug Administration 2008 publication of guidance is:

1. FDTs should have an In vitro disintegrating time of approximately 30 sec or less (using United States Pharmacopeia disintegration test or equivalent).
2. Generally, the FDT tablet weight should not exceed 500 mg, although the combined influence of stable weight, size and component solubility all factor into the acceptability of an ODT for both patients and regulators.
3. The guidance serves to define the upper limits of the FDT category, but it does not replace the original regulatory definition mentioned.

1.1.1 Ideal Properties of Fast Dissolving Tablets:

- Require no water for oral administration.
- Should be harder and less friable.
- Have an acceptable taste masking property.
- Leave minimal or no residue in mouth
- Exhibit low sensitivity to environmental conditions (temperature and humidity).

1.1.2 Advantages of Fast Dissolving Tablets:

- Ease of administration to patients who cannot swallow like the bed-ridden, stroke victims and patients who refuse to swallow like geriatrics, paediatrics and psychiatrics.
- Good mouth feel property of FDTs helps to change the perception of medication than bitter pill particularly in paediatric patient.
- Beneficial in cases such as motion sickness, sudden episodes of allergic attack or coughing,

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where an ultra rapid onset of action required.

1.1.3 Limitations of FDTs:

- The tablets usually have insufficient mechanical strength. Hence, careful handling is required.
- FDT requires special packaging for proper stabilization and safety of stable product.

1.1.4 Selection of Drug Candidates FDTs:

Several factors must be considered when selecting drug candidates for delivery as FDT dosage forms. The ultimate characteristics of a drug for dissolution in the mouth and pre gastric absorption from FDTs include

- No bitter taste.
- Good solubility in water and saliva.
- Dose should be as low as possible.
- Small to moderate molecular weight.
- Partially non- ionized at oral cavity's p^H.

1.2 Selection of superdisintegrant:

Although the superdisintegrant primarily affects the rate of disintegration, when used at high levels it can also affect mouth feel, tablet hardness, and friability. Thus, several factors must be considered when selecting a superdisintegrant.

- Produce rapid disintegration when tablet meets saliva in the mouth.
- Be compactable enough to produce less-friable tablets.
- Produce good mouth feel to the patient. Thus, small particle is preferred to achieve patient compliance.
- Have good flow since it improves the flow ability of the total blend.

1.3 Techniques in preparation of fast disintegrating drug delivery system:

1. Freeze drying or Lyophilization
2. Spray drying
3. Moulding
4. Phase transition process
5. Melt granulation
6. Sublimation
7. Mass extrusion
8. Direct compression
9. Nanonization
10. Effervescent method

1. Freeze-Drying or Lyophilization:

In freeze-drying process, the water is sublimed from the product after it is frozen.

a. Zydus technology:

Zydus technology (ZT) is a patented technique; it utilizes a unique freeze-drying process to manufacture finished dosage units which significantly differ from conventional oral systems.

b. Lyoc technology:

Lyoc technology lyophilizes, or "freeze-dries" an aqueous solution, suspension, or emulsion of an API and excipients. Lyoc technology is compatible with CIMA taste-masking techniques, customized release, high dosing and fixed-dose combination products.

c. Quicksolv technology:

Quicksolvis a porous solid form obtained by freezing an aqueous dispersion/solution of the drug containing matrix and then drying it by removing the water using excess of alcohol (solvent extraction).

Advantages:

The major advantage of using this technique is that the tablets produced by this technology have very low disintegration time and have great mouthfeel due to fast melting effect.

Disadvantages:

- It is a relatively expensive and time consuming process.
- The product obtained is poorly stable and fragile, rendering conventional packaging unsuitable.

2. Spray-Drying:

The formulations contained hydrolyzed and unhydrolyzedgelatin as a supporting agent for the matrix, mannitol as a bulking agent and sodium starch glycolate / croscaramellose as a disintegrant. Disintegration and dissolution were further enhanced by adding an acid (e.g., citric acid) or an alkali (e.g., sodium bicarbonate). The suspension of above excipients was spray-dried to yield a porous powder which was compressed into tablets. Tablets manufactured by this method disintegrated in < 20 secs in an aqueous medium.

3. Moulding:

Moulded tablets invariably contain water-soluble ingredients due to which the tablets dissolve completely and rapidly. Following are the different tablet moulding techniques:

a. Compression Moulding Process
b. Heat-Moulding Process

4. Phase transition process:

This process is done by compressing powder containing two sugars alcohols. One with high and another with low melting point, and they are heated at a temperature between their melting point and then compressed finally in order to get the tablets.

5. Melt granulation:

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It is a unique method for the preparation of orodispersible tablets by incorporating superpolystate. They play a dual role as a binder that increases the physical resistance of the tablets and also as a disintegrants, which help the tablet to melt in the mouth, and solubilise rapidly leaving no residue in the mouth.

6. Sublimation:

In this process, subliming material 'camphor' is used. It was sublimed in vacuum at 80°C for 30 min after preparation of tablets.In conventional types, sometimes rapid disintegration does not occur. Therefore, in order to improve porosity, volatile substance camphor is added in the preparation, which gets sublimed from the formed tablet.

7. Mass extrusion:

In this technique, a blend of active drug and other ingredients is softened using solvent mixture of water soluble polyethylene glycol, using methanol and then softened mass is extruded through the extruder or syringe to get a cylinder of product, which is finally cut into even segments with the help of heated blades to get tablets. The dried cylinder can be used to coat the granules of bitter tasting drugs and thereby masked their bitter taste.

8. Direct compression:

This is most popular technique because of its easy implementation and cost-effectiveness. The basic principle involves addition of disintegrates and water soluble excipients or effervescent agents. Superdisintegrates in optimum concentration (about 2- 5%) are mostly used so as to achieve rapid disintegration along with the good mouth feel.

9. Nanonization:

This technology involves reduction in the particle size of drug to nanosize by milling the drug using a proprietary wet-milling technique. Advantages of this technology include fast disintegration of nanoparticles leading to increased absorption and hence higher bioavailability and reduction in dose, cost effective manufacturing process.

10. Effervescent method:

Orodispersible tablets are also prepared by effervescent method by mixing sodium bicarbonate and tartaric acid of concentration 12% (w/w) along with super disintegrants like pregelatinized starch, sodium starch glycolate, crosspovidone and Croscarmellose. First, sodium bicarbonate and tartaric acid were preheated at a temperature of 80°C to remove absorbed/residual moisture and thoroughly mixed in the motor. Finally, the blends are compressed in the punch.

1.4. MECHANISM OF DISINTEGRATIONS BY SUPERDISINTEGRANTS There are five major mechanisms for tablet disintegration as follows:-

- **Swelling**

Swelling is believed to be a mechanism in which certain disintegrating agents (such as starch) impart the disintegrating effect. By swelling in contact with water, theadhesiveness of other ingredients in a tablet is overcome causing the tablet to fall apart.

E.g. Sodium starch glycolate, PlatagoOvata .

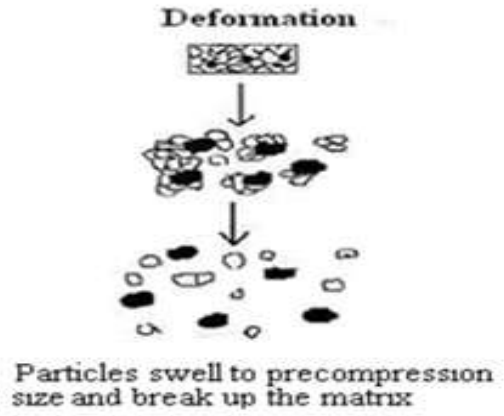

Fig.1. Mechanism of superdisintegrants by swelling

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➢ **Porosity and Capillary Action (Wicking)**

Effective disintegrants that do not swell are believed to impart their disintegrating action through porosity and capillary action. Tablet porosity provides pathways for the penetration of fluid into tablets. The disintegrant particles (with low cohesiveness & compressibility) themselves act to enhance porosity and provide these pathways into the tablet. Liquid is drawn up or "wicked" into these pathways through capillary action and rupture the interparticulate bonds causing the tablet to break apart.

E.g.Crospovidone,Crosscarmillose

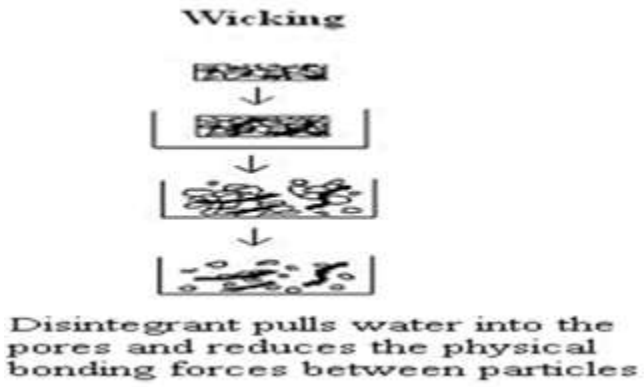

Fig.2. Disintegration of Tablet by Wicking

➢ **Deformation**

Starch grains are generally thought to be "elastic" in nature meaning that grains that are deformed under pressure will return to their original shape when that pressure is removed. But, with the compression forces involved in tableting, these grains are believed to be deformed more permanently and are said to be "energy rich" with this energy being released upon exposure to water. In other words, the ability for starch to swell is higher in "energy rich" starch grains than it is for starch grains that have not been deformed under pressure.

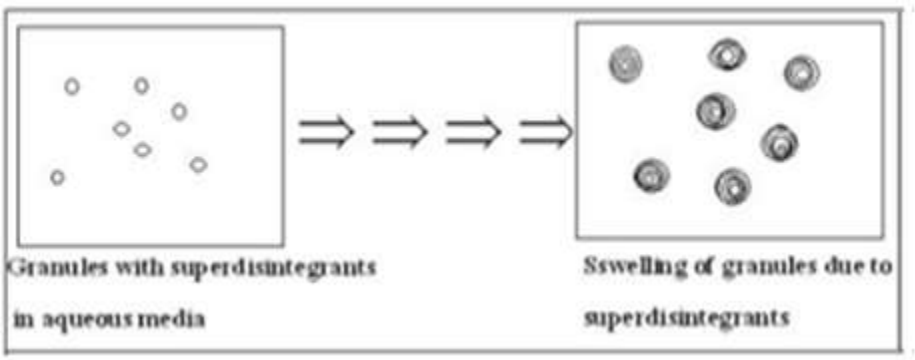

Fig.3. Disintegration by Deformation

➢ **Due to disintegrating particle/particle repulsive forces:-**

Another mechanism of disintegration attempts to explain the swelling of tablet made with „nonswellable" disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that nonswelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking. It is believed that no single mechanism is responsible for the action of most disintegrants. But rather, it is more likely the result of inter-relationships between these major mechanisms.

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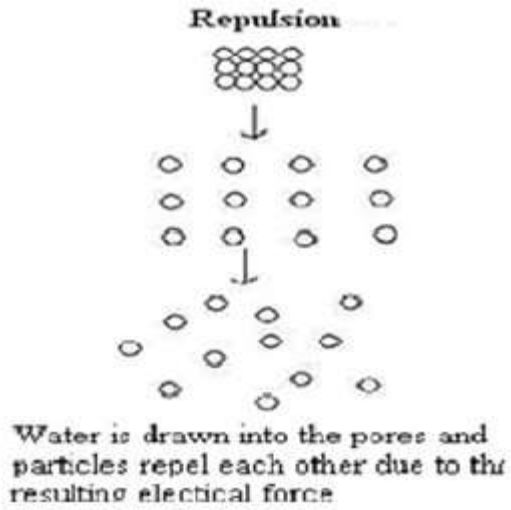

Fig 4: Disintegration by Repulsion

➢ **By Enzymatic Reaction:**

Enzymes present in the body also act as disintegrates. These enzymes dearth the binding action of binder and helps in disintegration. Due to swelling, pressure is exerted in the outer direction that causes the tablet to burst or the accelerated absorption of water leads to an enormous increase in the volume of granules to promote disintegration.

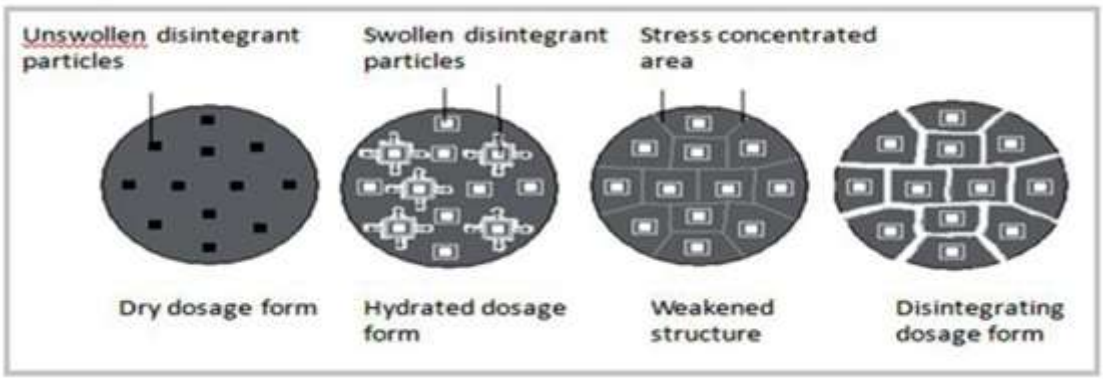

Fig.5. Disintegration mechanism of superdisintegrant materials

LITERATURE REVIEW

Literature review to understand the present and the past scenario of the fast disintegrating tablets prepared by different methods. The study was done by referring to various national and international journals, published articles in various official standard books and referring to various scientific websites.

Fast dissolving tablets of diclofenac potassium were prepared by direct compression method using Indion 214, Indion 234, Indion 244 and croscarmellose as superdisintegrants. Microcrystalline cellulose was used as diluents and mannitol, as sweetening agent. Weight variation of all the formulations was observed which were within the acceptable limit for uncoated tablets as per United States Pharmacopoeia. Indion 244 was found to have super disintegrant property the addition technique is a best method for preparing fast dissolving tablets for rapid pain management

Fast-disintegrating tablets (FDTs) of diclofenac potassium with sufficient integrity as well as a pleasant taste, using two different fillers and binders: Tablettose 70(®) and Di-Pac (®) have been prepared with direct compression method and evaluated. Results showed that FDTs of diclofenac

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potassium with durable structure and desirable taste can be prepared using both fillers and binders but tablets prepared with Di-Pac had a better taste so the tablet formulation containing Di-Pac was chosen for in vivo experiments. Placebo controlled in vivo trial demonstrated that 50 mg diclofenac potassium, administered as a single dose of FDTs or commercial tablets, was effective in relieving the pain and both of them were superior to placebo.

Malviyaet al ,(2012) have prepared mouth dissolving tablets of Diclofenac sodium using cucurbit maxima pulp powder as disintegrant by using wet granulation technique and microcrystalline cellulose as Filler

Vijay Sharma et al ,**(1997),**reported modified polysaccharide as fast disintegrating excipients for orodispersible tablets. Modified polysaccharide co-grinded treated agar and co-grinded treated agar and co-grinded treated gaur gum were prepared by subjecting pure polysaccharides of agar and guar gum to the sequential processes[15]

Mitesh Nagar et al., (2009):developed mouth dissolving tablets of cinnarzine, they utilized Chitosan Superdisintegrant property to develop a fast mouth dissolving tablet by utilizing a novelmethod of treatment which can replace any other superdisintegrant. The properties of the rapidlydispersible tablet, such as porosity, hardness, disintegration time, wetting time and dissolution time,were investigated. In conclusion, they succeeded in confirming that the preparation methoddesigned in this research is scalable, industrially applicable and useful for the preparation of ODTs containing drugs with poor solubility and poor bioavailability

Shrotriya SN, Patwardhan SK, Pundit AP, Khandelwal AP, More KS and Jain KS have developed dispersible tablets of diltiazem HCL employing varying concentration and of mucilage isolated from plant linumusitatissimum and of mucilage isolated from plant of linumusitatissimum (linseed) as a disintegrant. The disintegrating efficiency of separated mucilage has been compared with starch as a disintegrant in the formulated tablet. The tablet containing 8% linseed mucilage has shown less disintegration time and rapid drug release. The study has revealed the effectiveness of linseed mucilage powder in low concentration as disintegrant compared to starch19.

Nagendrakumaret al.,(2010) developed fast disintegrating tablets of fexofenadine HCL by effervescent method with a view to enhance patient compliance. Crosspovidine was used as super disintegrant. Croscamellose sodium, sodium starch glycolate along with sodium bicarbonate and anhydrous citric acid in different ratios were used by direct compressible mannitol (Pearlitol-SD200) to enhance mouth feel. Three formulations were tested for in vitro drug release pattern in p^H 6.8 phosphate buffer, short term stability at 40%, 75% RH for 3months.

Kamal sarohaet al., (2013) were studied the formulation and evaluation of fast dissolving tablets of Amoxicillin trihydrate using synthetic superdisintegrant. In present study, the fast dissolving tablets of Amoxicillin Trihydrate were prepared by direct compression technique using microcrystalline cellulose (MCC) as direct compressible diluents. Sodium starch glycolate(SSG) and crosscarmellose sodium (CCS) used as synthetic superdisintegrants. The swelling indices of the superdisintegrants were also compared. Among both the superdisintegrants, crosscarmellose sodium showed the highest swelling index. The blends showed satisfactory flow properties. Eight formulations were prepared using different concentrations of superdisintegrants and were investigated for their effect on the disintegration time and dissolution rate of the tablets. Tablets were also evaluated for weight variation, hardness, thickness, friability and drug content. All the tablets exhibited acceptable pharmaco-technical properties.

SudheshnababuSukhavasiet al., (2012) were studied the formulation and evaluation of fast dissolving tablets of amlodipine besylate by using Fenugreek seed mucilage and Ocimumbasilicum gum. The main aim of the present study was to formulate the fast dissolving tablets of amlodipine besylate tablets using Fenugreek seed mucilage and Ocimumbasilicum gum as a natural superdisintegranting agents to achieve quick onset of action, is to increase the water uptake with in shortest wetting time and there by decrease the disintegration time of the tablets by simple and cost effective direct compression technique. Pre-compression parameters like angle of repose and post compression parameters like wetting time, water absorption ratio, in-vitro dispersion time were studied.

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anhydrous citric acid in different ratios were used by direct compressible mannitol (Pearlitol-SD200) to enhance mouth feel. Three formulations were tested for in vitro drug release pattern in p^H 6.8 phosphate buffer, short term stability at 40%, 75% RH for 3months.

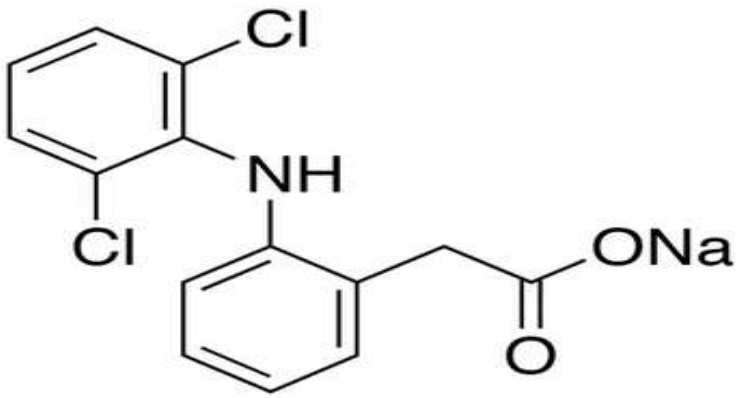
Patraet al.,(2008) prepared metronidazole mouth dissolving tablets using superdisintegrants like crosspovidone, indion 424, L-hpc and pregelatinised starch in various concentrations like 8% and 10% w/w by wet granulation method. All formulations were evaluated for physical characteristics of compressed tablets such as weight variation, hardness and friability. Formulations were evaluated for drug content, disintegrating time, in vitro dissolution studies. Among all the formulations, Formulation(containing 10% w/w concentration of crosspovidone) showed the disintegration time of 27 seconds, hardness 2.56 Kg/cm^3 which was considered as the best batch. All formulations followed Higuchi order kinetics.

Mahajan et al.,(2007) developed mouth dissolving tablets of sumartripan Succinate. They were prepared using disintegrants like sodium starch glycolate, carboxy methyl cellulose and treated with agar by direct compression method. They were evaluated for thickness, uniformity of weight . Water absorption ratio, in vitro, in vivo disintegration time and in vitro drug release. The tablets disintegrated in vitro and in vivo within 12 to 18 seconds.

II. MATERIALS AND METHODS

2.1 Drug description:

Chemical formula:C14H10Cl2NO2.Na
IUPAC Name-: 2-(2-(2, 6-dichlorophenylamino) phenyl) acetic acid, sodium.
Synonym: 2-[(2, 6-Dichlorophenyl)-amino]-benzeneacetic Acid, Sodium



Generic name: Soludol Tablet
Trade names: Aclonac , Cataflam, Flector ,· Pennsaid,Zipsor ·
Melting point: 281-284° C
Molecular weight: 318.1 g/mol.
Category: Anti-inflamatory agent (NSAID'S)
Discription: Odourless, yellowish-white, crystalline powdersparingly soluble in water
Standards: Diclofenac Sodium contains not less than 99.0% and not more than 101.0% of diclofenac sodium.
Loss on Drying: Not more than 0.5% of its weight
Stability and Storage: **Tablets:** Tight containers at ≤ 30°C.
Gel: 25°C (may be exposed to 15 – 30°C). Do not freeze.
Transdermal System: 25°C (may be exposed to 15 – 30°C).

2.2 Mechanism of action:

The exact mechanism of action is not entirely known, but it isthought that the primary mechanism responsible for its anti-inflammatory, antipyretic,and analgesic action is inhibition of prostaglandin synthesis by inhibition ofcyclooxygenase (COX). It also appears to exhibit bacteriostatic activity by inhibitingbacterial DNA synthesis.
Mechanism of action The anti-inflammatory effects of diclofenac are believed to be due to inhibition of both leukocyte migration and the enzyme cyclooxygenase (COX-1 and COX-2), leading to the peripheral inhibition of prostaglandin synthesis. As prostaglandins sensitize pain receptors,

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inhibition of their synthesis is responsible for the analgesic effects of diclofenac. Antipyretic effects may be due to action on the hypothalamus, resulting in peripheral dilation, increased cutaneous blood flow, and subsequent heat dissipation.

2.3Pharmacological information:
Diclofenac sodium, a nonsteroidal compound, exhibits pronounced antirheumatic, antiinflammatory,analgesic and antipyretic properties.

Inhibition of prostaglandin biosynthesis, is regarded as having an important bearing on its mechanism of action. Prostaglandins play a major role in the causation of inflammation, pain and fever. In rheumatic diseases, the anti-inflammatory and analgesic properties of DICLOFENAC elicit a clinical response characterised by relief from signs and symptoms such as pain at rest, pain on movement, morning stiffness, and swelling of the joints, as well as by an improvement in function.

In addition, clinical studies have revealed that in primary Dysmenorrhoea, diclofenac preparations are capable of relieving the pain and reducing the extent of bleeding.

2.4 Pharmacokinetics Profile:
2.4.1. Absorption:
Bioavailability: It is well absorbed following oral administration. It undergoes first-pass metabolism; Only 50–60% of a dose reaches systemic circulation as unchanged drug.
Peak plasma concentration usually attained within about 1 hour (diclofenac potassiumconventional tablets), 2 hours (diclofenac sodium delayed-release tablets), or 5.25 hours (diclofenac sodium extended-release tablets). Absorbed into systemic circulationfollowing Topical administration as gel or Transdermal system; plasma concentrations generally very low compared with oral administration.

Onset: Single 50- or 100-mg doses of diclofenac potassium provide pain relief within 30minutes.

Duration: Pain relief lasts up to 8 hours following administration of single 50- or 100-mgdoses of diclofenac sodium.

Food: Food delays time to reach peak plasma concentration but do not affect extent of absorption following administration as conventional, delayed-release, or extended-release tablets.

2.4.2. Distribution:
Extent: Following oral administration, concentrations in synovial fluid may exceed those in plasma.

Plasma Protein Binding: >99%.

2.4.3. Metabolism:
Metabolized in the liver via hydroxylation and conjugation. Somemetabolites may exhibit anti-inflammatory activity.

2.4.4. Elimination:
Elimination Route: Excreted in urine (65%) and in feces via biliary elimination (35%) as metabolites

Half-life: Oral preparations: 1–2 hours. Diclofenac epolamine transdermal system:approximately 12 hours.

2.4.5.Special Populations:
In geriatric patients, pharmacokinetic profile similar to that in younger adults.In patients with renal impairment, plasma clearance not substantially altered, althoughclearance of metabolites may be decreased.

2.5.Pharmacodynamic Profile:
2.5.1Drug Category
• Anti-Inflammatory Agents, Non-Steroidal
• Inhibits cyclooxygenase-1 (COX-1) and COX-2s
• Nonsteroidal anti inflammatory agent (NSAID's)

2.5.2Interaction With Other Medicines:
Lithium/Digoxin: When given together with preparations containing lithium or digoxin , Dclofenac may raisetheir plasma concentrations and these concentrations should be monitored during treatment with GN-DICLOFENAC.

Selective serotonin reuptake inhibitors (SSRIs): Concomitant administration of systemic NSAIDs including diclofenac and SSRIs mayincrease the risk of gastrointestinal bleeding.

Antidiabetics: Diclofenac can be given together with oral antidiabetic agents without influencing

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theirclinical effect. However there are isolated reports of both hypoglycaemic andhyperglycaemic effects in the presence of diclofenac, which necessitated changes in thedosage of hypoglycaemic agents. For this reason, monitoring of the blood glucose level is recommended as a precautionary measure during concomitant therapy.

Methotrexate: Caution should be exercised when NSAIDs including diclofenac are administered less than24 hours before or after treatment with methotrexate, since the blood concentration ofmethotrexate may rise and the toxicity of this substance be increased.

Phenytoin : When using phenytoin concomitantly with diclofenac, monitoring of phenytoin plasmaconcentrations is recommended due to an expected increase in exposure to phenytoin

Cyclosporin and Glucocorticoids: Increased nephrotoxicity of ciclosporin may occur through effects of NSAIDs including diclofenac on renal prostaglandins. Therefore, diclofenac should be given at doses lower than those that would be used in patients not receiving cyclosporin. The addition of glucocorticoids to NSAIDs, though sometimes necessary for therapeutic reasons, mayaggravate gastrointestinal side effects

Other NSAIDs: Other non steroidal anti-inflammatory drugs and corticosteroids. The concomitant use of diclofenac with systemic NSAIDs including cyclooxygenase-2 selective inhibitors, should be avoided due to the absence of any evidence demonstrating synergistic benefits and the potential for additive undesirable effects

2.5.3. Indications: Inflammatory and degenerative forms of rheumatism; rheumatoid arthritis, osteoarthritis. Relief of acute or chronic pain states in which there is an inflammatory component. Symptomatic treatment of primary dysmenorrhoea

2.5.4:Contraindications:

• History of allergic reactions (bronchospasm, shock, rhinitis, urticaria) followingthe use of Aspirin or another NSAID
• Third-trimester pregnancy
• Active stomach and/or duodenal ulceration or gastrointestinal bleeding

• Inflammative intestinal disorders such as Crohn's disease or ulcerative colitis
• Severe insufficiency of the heart

• Recently, a warning has been issued by FDA not to use to treat patientsrecovering from heart surgery

• Severe liver insufficiency (Child-Pugh Class C)

• Severe renal insufficiency (creatinine clearance <30 ml/min)

• Caution in patients with preexisting hepatic porphyria, as diclofenac may trigger Attacks
• Caution in patients with severe, active bleeding such as cerebral hemorrhage
• NSAIDs in general should be avoided during dengue fever.
• On animals which after death may be eaten by vultures or other scavenging birds

2.5.5: Adverse Reactions:

• **Oral diclofenac :** abdominal pain or cramps, constipation, diarrhea, flatulence, GI bleeding, GI perforation, peptic ulcer, vomiting, dyspepsia, nausea, dizzinessheadache, liver function test abnormalities, renal function abnormalities, anemia,prolonged bleeding time, pruritus, rash, tinnitus, edema.
• **Diclofenac sodium 1% gel:** application site reactions (e.g., dermatitis).

• **Diclofenac epolamine transdermal system**: application site reactions (e.g.,pruritus, dermatitis), nausea, altered taste.

Dermatological:. More than 1%: rashes or skin eruptions. Less than 1%:urticaria. In isolated cases: bullous eruptions, eczema, erythema multiform, Stevens-Johnson syndrome, Lyell's syndrome (acute toxic epidermolysis), erythroderma (exfoliative dermatitis), loss of hair, photosensitivity reaction, purpura, including allergic purpura, pruritus.

Renal:. Less than 1%: oedema

In isolated cases: acute renal failure, urinary abnormalities such as haematuria, proteinuria,interstitial nephritis, nephrotic syndrome, papillary necrosis.

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Hepatic: Up to 2%: elevation of serum aminotransferase enzymes (ALT, AST). Less than1%: hepatitis with or without jaundice. In isolated cases: fulminant hepatitis, hepatic necrosis, hepatic failure.
Central nervous system: More than 1%: headache, dizziness or vertigo. Less than 1%:drowsiness. In isolated cases: disturbances of sensation, including paraesthesia, memory disturbance, disorientation, disturbances of vision (blurred vision, diplopia), impaired hearing, tinnitus, insomnia, irritability, convulsions, depression, anxiety, nightmares, tremor,psychotic reactions, taste alteration disorders, cerebovascular accident, myoclonic encephalopathy (described in two patients), aseptic meningitis.

Haematological:. In isolated cases: thrombocytopenia, leucopenia, anaemia (haemolytic anaemia, aplastic anaemia), agranulocytosis, positive Coombs' test.
Hypersensitivity: Less than 1% bronchospasm; anaphylactic/anaphylactoid systemic reactions, including hypotension.

In isolated cases: vasculitis, pneumonitis.

Other: In isolated cases: impotence (association with diclofenac intake is doubtful),palpitation, chest pain, hypertension, cardiac failure, myocardial infarction, congestive heart failure, asthma. Toxic shock syndrome has been reported in patients administered NSAIDs postoperatively.

2.5.6:PRECAUTIONS:
Use with caution in the following circumstances-
Cardiovascular Thrombotic Event: Observational studies have indicated that non-selective NSAIDS may be associated with an increased risk of serious cardiovascular events, including myocardial infarction and stroke, which may increase with dose or duration of use.Patients with cardiovascular disease or cardiovascular risk factors may also be at greater risk.To minimize the potential risk of an adverse cardiovascular event in patients taking anNSAID, especially in those with cardiovascular risk factors, the lowest effective dose shouldbe used for the shortest possible duration (see Dosage and Administration).
Hypertension : NSAIDs may lead you to the onset of new hypertension or worsening of preexisting hypertension and patients taking anti-hypertensives with NSAIDs may have animpaired anti-hypertensive response. Caution is advised when prescribing NSAIDs topatients with hypertension. Blood pressure should be monitored closely during initiation ofNSAID treatment and at regular intervals there after.
Heart failure : Fluid retention and oedema have been observed in some patients taking NSAIDs, including diclofenac,therefore caution is advised in patients with fluid retention or heart failure.

Pre-existing asthma: In patients with asthma, seasonal allergic rhinitis, swelling of the nasalmucosa (i.e. nasal polyps), chronic obstructive pulmonary diseases or chronic infections ofthe respiratory tract (especially if linked to allergic rhinitis-like symptoms), reactions to NSAIDs such as asthma exacerbations (so called intolerance to analgesics/ analgesics asthma), Quincke's oedema or urticaria are more frequent than in other patients. Therefore, special precaution is recommended in such patients. This is applicable as well for patients who are allergic to other substances, e.g. with skin reactions, pruritus or urticaria.

Hepatic function: Close medical surveillance is required when prescribing DICLOFENAC GA to patients with impaired hepatic function, as their condition may be exacerbated.

Hypersensitivity: As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, have been reported with diclofenac. These reactions can occur without earlier exposure to the drug.

Lactose:DICLOFENAC-GA tablets contain lactose and therefore are not recommended for patients with rare hereditary problems of galactose intolerance, severe lactase deficiency or glucose/ galactose malabsorption.

Use in the elderly: In addition to the above precautions, in elderly patients who are generally more prone to side effects, particular caution should be exercised. It is recommended that the lowest effective dosage be used in elderly patients or those with a low bodyweight. Effects on ability to drive or use machines - Patients experiencing visual disturbances, dizziness, vertigo, somnolence or other CNS disturbances should refrain from driving a vehicle or operating machines.

Effects on fertility: The use of DICLOFENAC-GA may impair female fertility and is not

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recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of DICLOFENAC-GA should be considered.

Use in pregnancy: NSAIDs have an inhibitory effect on prostaglandin synthesis and, when given in the latter part of pregnancy, may cause premature closure of the fetal ductus arteriosus, foetal/renalimpairment, inhibition of platelet aggregation and delayed labour and birth.
The safety of diclofenac sodium in pregnancy has not been established. Therefore Diclofenac should not be used in pregnant women or those likely to become pregnant unlUse of DICLOFENAC-GA during the third trimester of pregnancy is contraindicated owing to the possibility of uterine inertia and/or premature closure of the ductus arteriosus

Use in lactation: Following oral doses of 50 mg administered every eight hours, the active substance passes into the breast milk. As with other drugs which are excreted in milk, diclofenac is notrecommended for use in lactation

Use in children: Diclofenac is not recommended for use in children as safety and efficacy in this age grouphave not been established

Infection: Like other NSAIDs, diclofenac may mask the usual signs and symptoms of infection due to its pharmacodynamic properties

Haematological effects: Like other NSAIDs, diclofenac may temporarily inhibit platelet aggregation. Patients with haemostatic disorders should be carefully monitored. During prolonged treatment, a slight reduction in haemoglobin has been noted in some patients. On rare occasions, blood dyscrasias have been reported. Periodic blood counts are therefore recommended.

2.6: Uses:
• Orally for symptomatic management of primary dysmenorrhea.

• For relief of mild to moderate pain.

• For relief of the signs and symptoms of symptomatic treatment of osteoarthritis rheumatoid arthritis and ankylosing spondylitis.

• For relief of the signs and symptoms of rheumatoid arthritis.

Diclofenac Systemic:
Brand Name: Voltaren ,Cataflam ,Cambia ,Zipsor
It is used in the treatment of:
- Back Pain
- Frozen Shoulder
- Migraine
- Period Pain
- Muscle Pain
- Rheumatoid Arthritis
- Aseptic Necrosis

Diclofenac Ophthalmic:
Brand Name: Voltaren Ophthalmic
It is used in the treatment of:
- Keratoconjuctivitis
- Corneal UlcerPostoperative Ocular Inflamation
- Conjunctivis

Diclofenac Topical:
Brand Name: VoltarenGel , Flector Patch , Pennsaid
It is used in the treatment of:

- Actinic Keratosis
- Osteoarthritis
- Pain

3.1 Excipients Used:

Table1: Excipients used

S.no	Ingredients	Category

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1.	Lactose	Diluents
2.	Mannitol	Sweetening agent
3.	Cross carmellose sodium	Super disintegrant
4.	Crospovidone	Superdisintegrant
5.	Sodium starch glycolate	Superdisintegrant
6.	Magnesium stearate	Lubricant
7.	Talc	Glidant

3.1.1.Diclofenac Na:

Diclofenac sodium is synthetic, nonsteroidal anti-inflammatory and analgesics compound. The mechanism responsible for its anti-inflammatory or antipyretics or analgesic action is inhibition of prostaglandin synthesis by inhibition of cyclooxygenase [COX]. Diclofenac may also be a unique member of the NSAIDs. It is well absorbed orally and shows 100% bioavailability, 99% protein bound, metabolized and excreted both in urine and biles and plasma t1/2 is 1-2 hours.

3.1.2 Mannitol:

Mannitol is a white, crystalline solid that looks and tastes sweet like sucrose. Mannitol has several industrial uses, but is mainly used to produce tablets of medicine. Mannitol is classified as a sugar alcohol; that is, it is derived from a sugar (mannose) by reduction.

3.1.3 Lactose:

Lactose is a disaccharide sugar that is found most probably in milk and is formed galactose and glucose. Lactose make up around 2-8% of milk, although the amount varies among the species and individuals.

Lactose is widely used as a filler or filler-binder in the manufacture of pharmaceutical tablets and capsules. Its band flavour has lent to its use as a carrier and stabiliser of aromas and pharmaceutical products.

3.1.4 Crosscarmellose sodium:

Crosscarmellose sodium is an internally cross-linked sodium carboxymethylcellulosefor use as a superdisintegrant in pharmaceutical formulations. The cross-linking reduces water solubility while still allowing the material to swell (like a sponge) and absorb many times its weight in water. As a result, it provides superior drug dissolution and disintegration characteristics, thus improving formulas′ subsequent bioavailability by bringing theactive ingredients into better contact with bodily fluids.

3.1.6 Sodium starch glycolate:

Sodium starch glycolate to capsules and tablets to help make them disintegrate and dissolve better, making it easier for your body to absorb the medication. It does this by absorbing water quickly so the pill swells and breaks apart into small pieces. It can also be used to help form gels.

3.1.7 Crospovidone:

Crospovidone use a combination of swelling and wicking. Due to its crosslink density, crospovidone swells rapidly in water without gelling. Crospovidone particles are found are found to be granular and highly porous which facilitates wicking of liquid into the tablet and particles to generate rapid disintegration.

3.1.8 Magnesium stearate:

Magnesium stearat**e**, also called octadecanoic acid, magnesium salt, is a white substance, powder which becomes solid at room temperature.

Magnesium stearate is often used as an anti-adherentin the manufacture of medical tablets, capsules and powders.It has lubricating properties,

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preventing ingredients from sticking to manufacturing equipment during the compression of chemical powders into solid tablets; magnesium stearate is the most commonly used lubricant for tablets.

3.1.9 Talc:

Talc is a mineral composed of hydrated magnesium silicate. In loose form, it is the widely used substance known as talcum powder. Talc finds use as a cosmetic (talcum powder), as a lubricant, and as filler in paper manufacture. Talc is also used as food additive or in pharmaceutical products as a glidant.

3.2Equipments used:

Equipments used in the formulation are listed below:

1. 16 STATION TABLET PUNCHING MACHINE
2. UV – VISIBLE SPECTROPHOTOMETER
3. DISSOLUTION APPARATUS

1.16 STATION TABLET PUNCHING MACHINE:

Single punch press can be divided into different types. Single- punch is driven by both motor and hand and is utilized for pressing tablets from a variety of granulated materials. Tablet punch machined is basically utilized for research and developments and in manufacturing of herbals, pharmaceuticals, nutraceuticals and other products. A tablet is formed by the collective pressing action of two punches and a die.

USES:

- For producing tablets
- Can produce tablets of diverse variety like pharmaceuticals, cleaning products, cosmetics.
- Varied kinds of tablets are formed from granular raw materials.
- Can be electronic motor driven as well as hand- operated.
- The filling depth of material and tablet's thinkness is adjustable.

Fig.6: 16 STATION TABLET PUNCHING MACHINE

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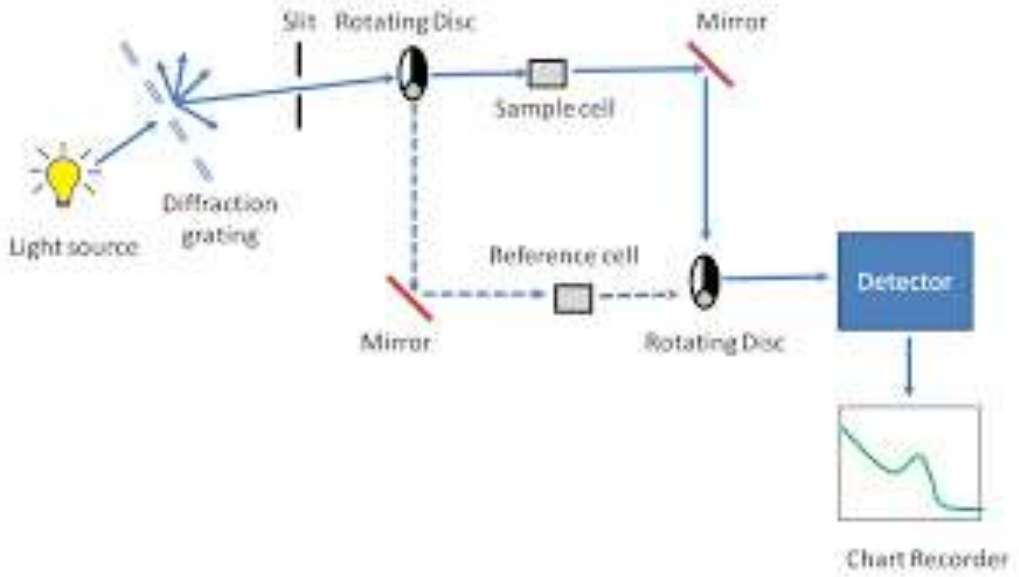
2. UV- VISIBLE SPECTROMETER



A) The light source:

A light source which gives the entire visible spectrum plus the near ultra- violet so that you are conveying the range from about 200 nm to about 800 nm (this extends slightly into the near infra- red as well). The combined output of these two bulbs is focused on to a diffraction grating.

B) The diffraction grating and the slit :

We are probably familiar with the way that a prism splits light into its component colors. A diffraction grating does the same job, but more efficiently.

The slit only allows light of a very narrow range of wave length through into the rest of the spectrometer.By gradually rotating the diffraction grating, we can allow light from the whole spectrum (a tiny part of the range at a time through into the rest of the instrument.

C) The rotating discs:

Each disc is made up of a number of different segments. Those in the machine we are describing have three different sections- other designs may have different number segments. The light coming from the diffraction grating and slit will hit the rotating disc and one of three things can happen.

1. If it hits the transparent section, it will go straight through and pass through the cell containing the sample. It is then bounced by a mirror onto a second rotating disc.
2. If the original beam of light from the slit hits the mirrored section of the first rotating disc, it is bounced down along the green path. After the mirror, it passes through reference cell.
3. If the light meets the first disc at the black section, it is blocked- and for a very short while no light passes through the spectrometer. This just allows the computer to make allowance for any current generated by the detector in the absence of any light.

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Fig 7: UV-Visible Spectrometer

D) The sample and reference cells:

These are small rectangular glass or quartz containers. They are often designed so that the light beam travels a distance of 1cm through the contents.

The sample cell contains a solution of the substance we are testing- usually very dilute. The solvent is chosen so that it doesn't absorb any significant amount of light in the wavelength range were interested in (200- 800 nm). The reference cell just contains the pure solvent.

E) The detector and computer:

The detector converts the light into a current. The higher the current, the greater the intensity of the light.

3. DISSOLUTION APPARATUS

Manufactured by: DRK instruments
DRK dissolution test apparatus

Description:

The dissolution apparatus used is 8-basket apparatus according to U.S.P i.e, ROTATING PADDLE TYPE OF APPARATUS [Hansen paddle type].
This method was first described by levy and haveys. This kind of assembly is normally prescribed to those drugs which are poorly water soluble and also provides more vigorous conditions to yield quick results. Paddle methods produces turbulence compared to basket method
An assembly of dissolution apparatus consists of following parts:

A) Cylindrical vessel :
Normally it is made of glass or other inert transparent material. It is spherical bottomed and contains a fanged lid. It has a normal capacity of 1000 ml.

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B) Variable speed motor:
The speed of the motor should be capable of being varied between 25-150 rpm and maintained with in 5% required speed. A basket is attached to the shaft of motor.

C) Paddle :
The paddle is attached to the motor through shaft and the paddle rotates with variable speed. The shaft is suitably positioned and rotates without significant wobble. It is coated with fluro carbon.

D)**Water bath:**
The cylindrical vessel is securely clamped in water bath. It is set to maintain the temperature of the dissolution medium in the vessel at 37 C.

Dissolution conditions for drug release study of Diclofenac tablets:

Temperature of the medium: 37 C. o

Dissolution medium: Phosphate buffer pH 7.4.

Volume of the dissolution medium: 900ml

Rotations of paddle/ min: 50 rpm

Fig 8: Dissolution test Apparatus

3.3Preformulation studies:
3.3.1 Angle of repose:
The friction forces in a loose powder can be measured by the angle of repose (θ). It is an indicative of the flow properties of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane.

$\tan(\theta) = h / r$
$\theta = \tan^{-1}(h / r)$
Where, ɵ is the angle of repose
h is the height in cms
r is the radius in cms.

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Table 2: Angle of Repose as an Indication of Powder Flow Properties

Sr. No.	Angle of Repose (°)	Type of Flow
1	< 20	Excellent
2	20 – 30	Good
3	30 – 34	Passable
4	> 34	Very Poor

3.3.2Bulk Density (D_b):

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below.

It is expressed in g/ml and is given by

$D_b = M / V_b$

Where,

M is the mass of powder,

$V_b$is the bulk volume of the powder.

3.3.3 Tapped Density (D_t):

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 100 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2 % (in a bulk density apparatus).

It is expressed in g/ml and is given by

$D_t = M / V_t$

Where,

M is the mass of powder,

V_t is the tapped volume of the powder.

3.3.4 Hausner's ratio:

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by following formula.

Hausner's ratio = D_t / D_b

Where,

D_t is the tapped density,

D_b is the bulk density.

Table 3: Relationship between flow characters and Hausner's ratio

Flow Character	Hausner's Ratio
Excellent	1.00-1.11
Good	1.12-1.18
Fair	1.19-1.25
Passable	1.26-1.34
Poor	1.35-1.45
Very Poor	1.46-1.59
Very Very Poor	>1.60

3.3.5 Compressibility index:

The compressibility index (Carr's Index) was determined by using following equation,

Carr's Index (%) = $[(D_t - D_b) \times 100] / D_t$

Where,

D_t is the tapped density of the powder

D_b is the bulk density of the powder.

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Table 4: Relationship between % compressibility and flow ability

% Compressibility	Flow ability
5-12	Excellent
12-16	Good
18-21	Fair passable
23-35	Poor
33-38	Very poor
< 40	Very very poor

3.5 Formulation development:

Table 5: Formula used in formulation of Diclofenac Na fast disintegrating tablets

Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)
Diclofenac Na	200	200	200	200	200	200
Sodium starch glycolate	30	50	_	_	_	_
Crosscarmellose sodium	_	_	30	50	_	_
Crosspovidone	_	_	_	_	30	50
Mannitol	250	250	250	250	250	250
Lactose	420	400	420	400	420	400
Magnesium stearate	50	50	50	50	50	50
Talc	50	50	50	50	50	50
Total	1000	1000	1000	1000	1000	1000

Method of formulation:

Fast disintegrating tablets of Diclofenac sodium containing different concentrations of super disintegrants were prepared by wet compression method all the ingredients without magnesium stearate and talc were sifted through the sieve #44 and are mixed for about 15min to make a uniform blend. Magnesium stearate and talc were passed through sieve #60 and mixed with above powder for sufficient time, usually 5-7mins.

The prepared powder were evaluated for various preformulation parameters like bulk density, tapped density ,angle of repose, carr's index and Haunser ratio and compressed using sixteen station rotary tableting machine. Finally all the evaluation tests were conducted.

3.6 Evaluation tests:

3.6.1 Weight variation:

Tablets are designed to contain a specific amount of drug in a specific amount of tablet

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formula; the weight of the tablet being made is routinely measured to help ensure that a tablet contains the proper amount of drug. Average weight of 20 tablets were selected randomly from the lot and weighed individually to check for weight variation.

Table 6: Weight Variation Limits for Tablets (I.P)

Average Weight of Tablet	% Deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5

3.6.2 Thickness:

The thickness of pre-weighed 10 tablets of each formula was measured using a micrometer. It is measured by placing it between two anvils and rotating the sliding knob until the tablet was tightly fitted and the reading was noted. The tablet thickness should be controlled within a ±5% variation of a standard value.

3.6.3 Hardness:

Hardness or tablet crushing strength, the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester. It is expressed in kg cm^2. Usual range of hardness for conventional tablets is 4-6 kg/cm^2. The hardness for FDTs should be preferably 2-3 kg/cm^2.

3.6.4 Friability (F):

Friability of the tablet is determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at a height of 6 inches in each revolution. Preweighed sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} 100$$

3.6.5 Wetting time:

A piece of tissue paper folded double was placed in a Petri plate (internal diameter is 6.5 cm) containing 6ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at 37°C.

3.6.6 Disintegration time:

According to this method, a Petri dish of 10cm diameter was filled with 10ml of distilled water, the tablet was carefully placed at the centre of the Petri dish, and the time necessary for the complete disintegration of the tablet into fine particles was noted as disintegration time.

3.6.7 Dissolution studies:

Tablet test condition for the dissolution rate studies were used according to USP specification using USP type II apparatus. The dissolution medium was 900 ml of phosphate buffer (pH 7.8). The temperature of the dissolution medium and the rate of agitation were maintained at $37^0 \pm 0.5^0$ C and 50 rpm respectively. Aliquots of 10 ml of dissolution medium were withdrawn at specific time intervals and the volume was replaced by fresh dissolution medium, pre warmed to $37^0 \pm 0.5^0$C. The drug concentration was determined spectrophotometrically at 282 nm using UV spectrophotometer.

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III. RESULTS AND DISCUSSIONS

4.1 Pre formulation studies:-

Table7: Flow properties

Code	Angle of repose(ɵ)	Bulk density ($gm/cm^{3.}$)	Tapped Density ($gm/cm^{3)}$	Carr's index(%)	Hausner Ratio
F_1	34.6	0.52	0.62	16.12	1.274
F_2	37.2	0.50	0.62	19.4	1.811
F_3	29.6	0.51	0.61	16.4	1.177
F_4	38.6	0.50	0.63	20.6	1.177
F_5	35.3	0.50	0.60	19.4	1.178
F_6	35.7	0.48	0.58	20.5	1.787

Organoleptic and flow properties-:

Various Organoleptic and flow properties studies have been done and the results are based on standard given. Therefore preformulation values are within the limits.

4.2Evaluation tests of Diclofenac Sodium fast disintegratingtablets:-

Table8: Evaluation tests of Diclofenac Sodium fast disintegrating tablets

Code	Hardness (kg/cm^2)	Thickness (cm)	Friability%	Weight variation(mg)	Wetting time(sec)	Disintegration time (sec)
F_1	4.52	2.71	0.54	1.8	79sec	24sec
F_2	4.96	2.68	0.26	2.3	74sec	28sec
F_3	4.60	2.70	0.58	2.4	75sec	25sec
F_4	4.80	2.75	0.47	2.2	49sec	28sec
F_5	4.41	2.77	0.62	1.9	34sec	29sec
F_6	4.50	2.84	0.65	2.1	52sec	33sec

- The hardness was found to be in the range of 2.5 to 3.0 kg/cm^3.
- Tablet thickness was maintained between 2.14 to 2.86cm.
- The friability was found to less than 1% was indication of good mechanical resistance of tablets.
- As the powder was free flowing tablets produced were of uniform weight with acceptable weight variation (≤ 1.19%) due to uniform die fill.

4.3Standard graph of Diclofenac Sodium:

Table 9: Standard graph of Diclofenac sodium

Concentration(µg/ml)	Absorbance
0	0
5	0.14

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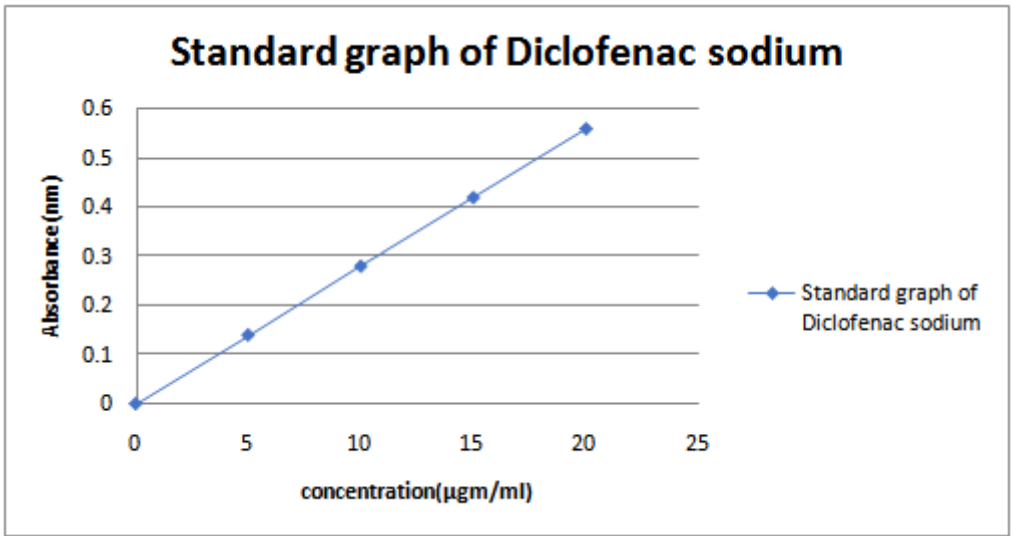
10	0.28
15	0.42
20	0.56
25	0.71

The absorbance of above solutions was recorded at λ_{max}(282nm) of the drug using double beam UV -visible spectrophotometer. Standard graph was plotted between the concentration X-axis) and absorbance (on Y-axis).



Graph 1: Graph plotted between concentration and absorbance

A spectrum of the working standards was obtained by scanning from 200-400nm by UV double beam spectrophotometer against the reagent blank to fix absorption maxima. The $\lambda_{max}$was found to be 282nm .Hence all further investigation were carried out at same wavelength. After conducting a number of trials, the concentration range which obeyed Beer's law was found to be between 0-100µg/ml. A calibration curve was conducted, which had a slope of 0.028.

4.4 In vitro drug release studies:

In vitro drug release profiles of Diclofenac from the Formulation ODT Tablets .

Sodium starch glycolate:

Table 10: In vitro drug release of Diclofenac with Sodium starch glycolate

Time(in mins)	**% drug release**	
	F_1	**F_2**
0	0	0
15	40.4	37.2
30	47.6	50.6

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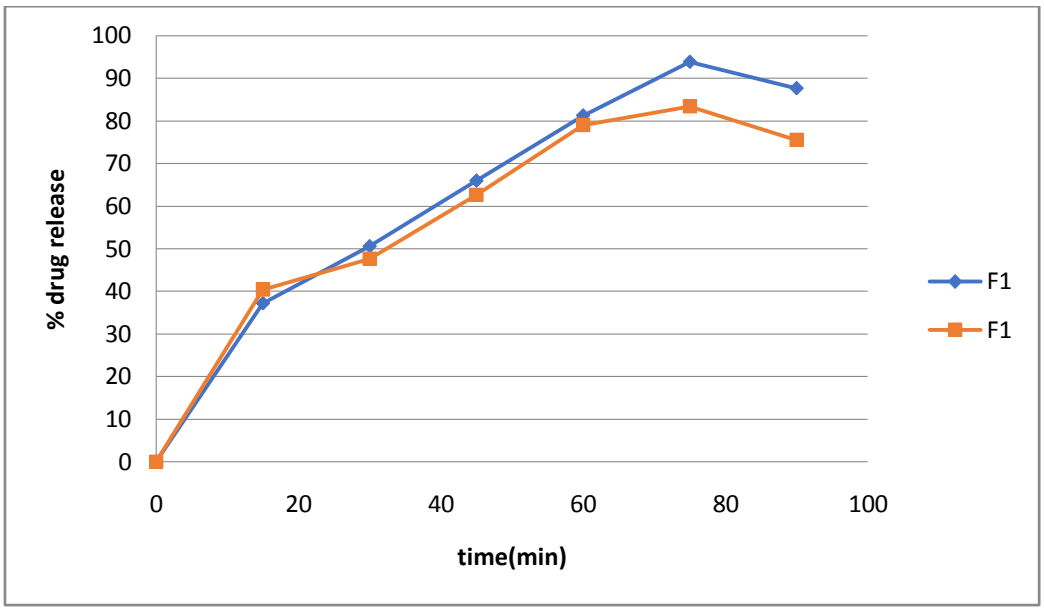
45	62.6	66
60	79	81.3
75	83.4	93.9
90	75.5	87.7



Graph 2:Graph plotted between concentration and absorbance with SSG

Crosscarmellose sodium:

Table 11: In vitro drug release of Diclofenac with crosscarmellose sodium

Time(in mins)	**% Drug Release**	
	F_3	**F_4**
0	0	0
15	46.8	37.2
30	52.7	48.0
45	66.0	52.2
60	85.5	82.6
75	86.6	47.3
90	45	41.7

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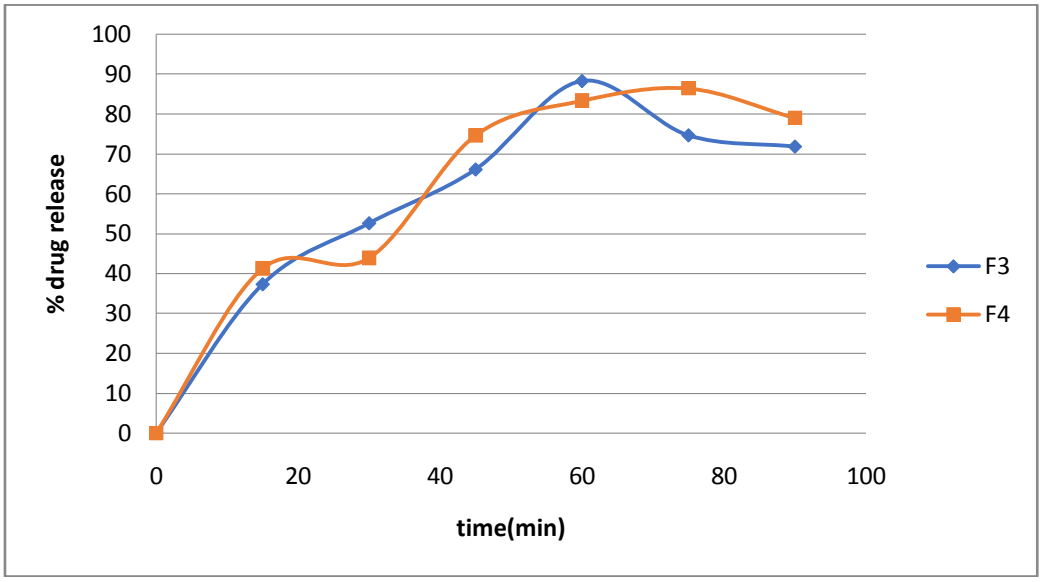

Graph 3: Graph plotted between concentration and absorbance with CCS

Crospovidone:

Table12: Invitro drug release of Diciofenac with crospovidone.

Time(in mins)	% Drug Release	
	F_5	F_6
0	0	0
15	37.3	41.26
30	52.46	43.9
45	66.08	74.6
60	88.26	83.3
75	74.64	86.4
90	71.82	79

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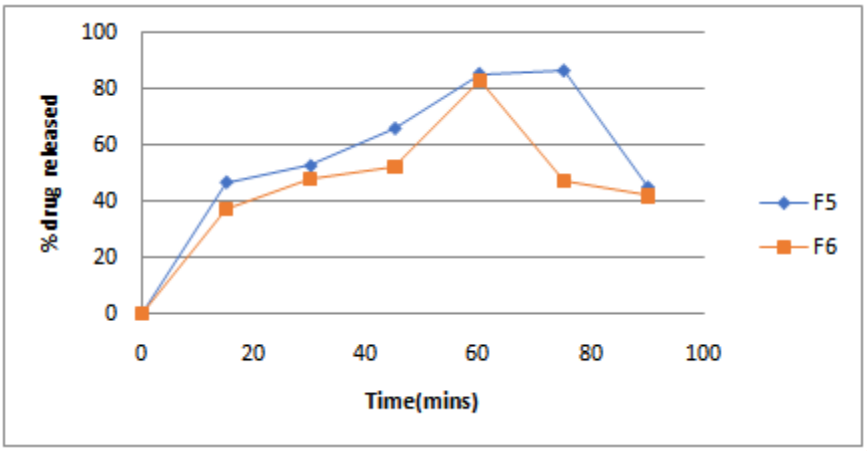

Graph 4: Graph plotted between concentration and absorption with crospovidone.

IV. CONCLUSION

Fast disintegrating tablets have potential advantages over conventional dosage forms, with improved patient compliance, convenience, bioavailability and rapid onset of action. They are a very good alternative for drug delivery to geriatric and paediatric patients. They have significant advantages of both solid and liquid dosage forms, as they remain solid during storage, which aid in stability of dosage forms and transform into liquid form within few seconds after its administration. As a result of the variety of technologies for its formulation, several commercial products are available in the market. Thus FDT has tremendous scope for being the delivery system for most of the drugs in near future.

All the formulation was evaluated for bulk density, tapped density, Hauser's ratio, compressibility index and angle of repose. As the powder was free flowing, tablets produced were of uniform weight with acceptable weight variation (≤1.19%) due to uniform die fill. Thus the observation of the study can be summarized as

- Tablet prepared by wet granulation method were found to be good, without any chipping, sticking and capping.
- The hardness was found to be in the range of 2.5 to 3.0 kg/cm^3.
- Tablet thickness was maintained between2.14 to 2.86 cm.
- The friability was found to less than 1% was indication of good mechanical resistance of tablets.

It is concluded that the formulated fast disintegrating tablets of Diclofenac using sodium starch glycolate was capable of exhibiting immediate release properties. Among all the formulations F-1 prepared with sodium starch glycolate in concentration 3% as super disintegrant exhibit least disintegration time(24 sec) and showed maximum drug release of 93.9% within 75 minutes.

As the concentration of super disintegrant in the formulations increased the disintegration time was found to decrease. From the characterisation of fast disintegrating tablets of Diclofenac it can be concluded that formulation containing sodium starch glycolate 3% is most acceptable.

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