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## Development and description of mouth-dissolving drug delivery system

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### Article History:

### Abstract



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### Keywords:

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Fast-dissolving oral films (FDOFs) offer superior comfort and flexibility as they dissolve in the oral cavity upon contact with saliva within minutes, enhancing the efficacy of active pharmaceutical ingredients (APIs) without the need for chewing or drinking. Epilepsy, a neurological disorder, requires prompt seizure management. Lamotrigine (LMG), a novel antiepileptic drug, treats various types of seizures. Complexing LMG with  $\beta$ -cyclodextrins enhances solubility and masks its bitter taste. Researchers developed and evaluated fast-dissolving lamotrigine films to improve palatability and bioavailability, aiming to shorten epileptic seizure duration. Nine initial formulations were created using a solvent-casting process. These formulations underwent rigorous evaluation for physico-chemical properties, including drug content, tensile strength, weight and thickness uniformity, folding endurance, elongation percentage, moisture content, in-vitro disintegration time, and dissolution characteristics. This study aims to enhance the effectiveness and patient acceptability of lamotrigine through innovative FDOF formulation techniques.

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### INTRODUCTION

The immune system's response to harmful stimuli such as infections, injured cells, toxic substances, or radiation is inflammation, which functions by removing harmful stimuli and starting the healing process. Important microcirculatory activities during the inflammatory phase include changes in vascular permeability, leukocyte recruitment and accumulation, and release of inflammatory mediators [1]. Inflammation has long been thought to be a part of innate immunity. The rush

of neutrophils leukocytes, rapidly followed by the influx of monocytes, causes redness, swelling, and discomfort at the site of damage. Monocytes develop into inflammatory macrophages, which multiply and affect cellular function. In contrast to adaptive immunity, the initiation and rapid onset of inflammation is mediated by receptors and involves four stages: a stimulus (sterile/ infection), radar that detects danger (receptors), signal transduction to the nucleus to initiate production of various mediators to combat the damage, and clearance of the stimuli [2]. The inflammatory response is the coordinated activation of signaling pathways that govern the amounts of inflammatory mediators in both resident tissue cells and blood-borne inflammatory cells. Many chronic diseases, such as cardiovascular and intestinal diseases, diabetes, arthritis, and cancer, are caused by inflammation [3].

### Causes of Inflammation

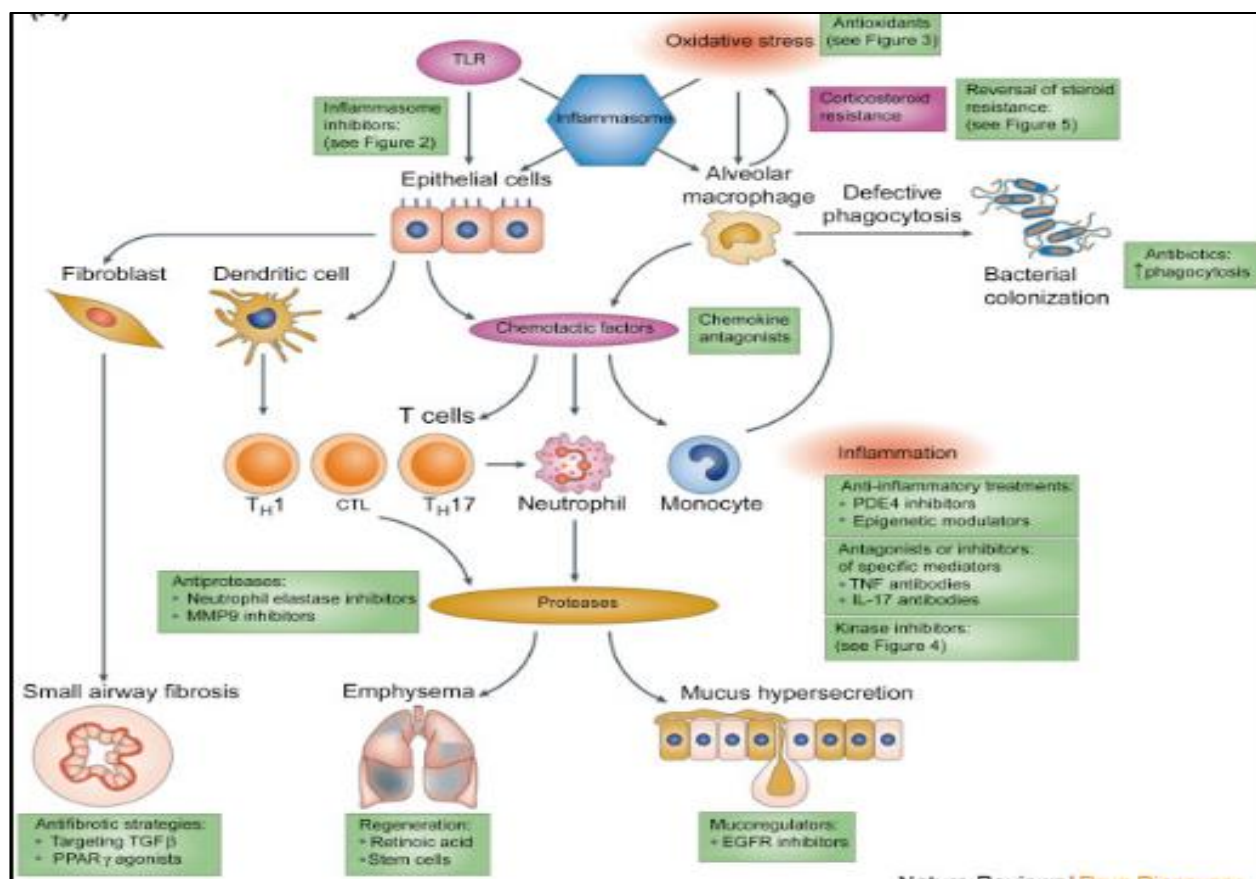
Inflammation appears to be a result of the following diseases:

1. Physical factors, including radiation, temperature changes, and mechanical traumas.
2. Chemical agents, which include the ever-growing lists of poisons and drugs [4].
3. Pathogenic agents (bacteria, viruses, fungi, and parasites).
4. Immunologic diseases, including immune deficiency conditions, autoimmunity, and hypersensitivity reactions [Figure 1].
5. Genetic and metabolic conditions, gout, diabetes, etc., are a few examples [5].

### MATERIAL AND METHODS

#### MATERIALS:

Fenoprofen is the gifted sample, and other polymer mixtures such as Ethanol, Methanol, Ethyl acetate, Chloroform, Hydrochloric acid, Sodium hydroxide, KCl solution,  $\beta$ -cyclodextrin, Tarteric acid, sodium starch glycolate, are from merck company, n-octanol, Phosphate Buffered Saline, Phosphate Buffered 6.8, and Phosphate Buffered 7.4 consists of Analytical grade.



**Figure 1 Mechanism of Chronic Inflammation**

## METHODS:

### Pre formulation study

The pre-formulation activity enhances the probability of successfully formulating a marketable product, gives a rational foundation for formulation approaches, and, in the end, serves as a foundation for optimizing drug product quality and performance. Pre-formulation is the study of the sustained release matrix tablet substance's physical and chemical characteristics by itself and in combination with an excipient. Since a step taken early saves nine, the new product's preformulation studies can save tragedies by preventing them before they happen [6].

### Drug-excipient interaction/ Compatibility study

#### Compatibility study by FTIR

An active pharmaceutical ingredient's (API) compatibility with some excipients currently in use is often evaluated by screening methods such as Fourier Transform Infrared Spectroscopy (FT-IR). FTIR gives information about chemical interactions between the excipient and the API by assigning spectral bands to each. Formulation scientists can use this process to learn which chemical groups in the excipients to avoid to promote the creation of more stable blends [7].

### Formulation study

#### Formulation: Preparation and characterization of ternary complex

##### Making ternary complexes

As explained below, ternary complexes of fenopropfen,  $\beta$ -cyclodextrin, and tartaric acid were synthesized at 1:2:2, 1:3:3, and 1:4:4 molar ratios, respectively [8].

##### The physical mixture (PM)

To create physical mixtures,  $\beta$ -cyclodextrin, tartaric acid, and fenopropfen were precisely weighed, mixed in a mortar using a trituration process, and then sieved using a 0.25-mm sieve. Up to a subsequent assessment, every physical mixture was kept in a desiccator [9].

##### Kneaded complex (K.C.)

A minimum ethanol/water mixture (15/85, V/V) was used to wet the physical mix in a mortar and

knead it thoroughly with a pestle to create a paste. This paste was then dried under vacuum at room temperature, sieved through a 0.25-mm sieve, and stored in a desiccator until further examination. This produced the kneaded complex of Fenopropfen,  $\beta$ -cyclodextrin, and tartaric acid [10].

##### Spray-dried complex (SDC)

Fenopropfen,  $\beta$ -cyclodextrin, and tartaric acid were combined and dissolved in ethanol and water (15/85, V/V). The resulting clear solution was stirred for 48 hours at room temperature to achieve complexation equilibrium using a magnetic stirrer. The following parameters were used to carry out the spray drying process using a laboratory-scale spray dryer: intake temperature of 112 °C, outlet temperature of 55 °C, atomization air pressure of 100 kPa, aspiration pressure of -2.5 kPa, and flow rate of 12 mL min<sup>-1</sup>. After passing through a 0.25-mm sieve, the powder sample was kept in a desiccator pending additional analysis [11].

##### Incision efficiency

The 25 mg kneaded complex was added to a 25 ml volumetric flask and 10 ml of methanol, thoroughly mixed, and sonicated for 30 minutes. Methanol was used to bring the volume up to par. The drug content of the solution was measured spectrophotometrically at 270 nm after it had been appropriately diluted with the same solvent [12].

##### Dissolution studies (I.P. 2010)

Using the USPXXIII apparatus (Electrolab India), dissolution studies were carried out in phosphate buffer (PH 6.8, 900 ml) at 37 $\pm$ 2°C. The paddle rotated at 50 rpm, containing 6.25 mg of drug. After the prescribed amount of time, samples were removed and filtered (Whatman filter paper no. 41), and the drug content was measured spectrophotometrically at 270 nm [13].

##### Preparation of tablet as per optimized formula

Making a mouth-dispersing tablet with a ternary complex of tartaric acid,  $\beta$ -cyclodextrin, and fenopropfen. This work used direct compression to make the 6.25 mg mouth-dissolving fenopropfen tablets. In each formulation, different concentrations of super disintegrants (sodium starch glycolate, crospovidone, and cross carmellose) were utilized (2%, 4%, 6%, 8%, and

10%). There were five different fenopufen formulations made. The primary sweetener utilized was sodium saccharine.

### Procedure

Each gradient was run through a #60 mesh individually. Every time, a tiny amount of the drugs, super disintegrant, and diluents were combined, blended, and put aside to create a homogenous combination. Weighed and combined in a geometrical order with the remaining ingredients. At this point, lubricant was thoroughly incorporated into the mixture. Utilizing a multistation tablet punching machine, the 300 mg tablets were created using direct compression [14].

### Evaluation of Blend Characteristics

#### Pre-composed evaluation parameter

##### Angle of repose [15]

The Angle of Repose was measured to determine the flow characteristic. After selecting the Angle of Repose, the flow attribute was ascertained. It is the most excellent angle that can be formed between a powder heap's free-standing surface and the horizontal plane.

$$\theta = \tan^{-1}(h/r)$$

##### Bulk density

##### Apparent bulk density

The material is funneled into a cylinder with a known volume to conduct the test. Calculating the apparent density involves dividing the material's weight by the cylinder's volume.

$$D = M/V$$

##### Tapped bulk density

Using a Pharma Test (PT-T.D) device, a measuring cylinder with a known sample volume was mechanically tapped to determine the tapped density. The cylinder was mechanically tapped 100 times in a minute after the initial volume was noted. The mass divided by the final tapped volume yields the tapped density.

Formula

$$D = M/V$$

##### Compressibility Index

The compressibility index (I) (flow ability) was measured to ascertain the flow property. Applying the compressibility index (I), provided by the below equation, provides a straightforward indication of the conditions under which a material can flow [16].

$$I = [1 - (V/V_0)] \times 100$$

### Morphological Characterization [17-23]

#### Hardness

By shattering the tablets between the second and third fingers and using the thumb as a pivot, the hardness of the tablet was ascertained. With a crisp crack, it was decided that the tablet's strength was sufficient.

#### Weight Variation

To conduct the USP weight variation test, each of the twenty tablets was weighed separately, the average weight was determined, and the weights of each tablet were compared to the average. The tablets satisfied the USP test, which stated that no tablet differed by more than twice the percentage limit and that no more than two tablets were outside the limit.

#### Disintegration

It is the process of breaking down tablets into smaller particles in a solution, termed disintegration. The selected drug's in vitro disintegration time was analyzed using a D.T. test instrument as per the Indian Pharmacopoeia Specification. Tablets were taken and put in each tube containing the baskets. The discs were placed on each tablet in the tubes and the instrument using the medium of 6.8 pH buffer and set the temperature at  $37.0 \pm 0.5^\circ\text{C}$  as in the medium. The disintegration time was noted.

#### Friability study

Roche Friabilator was used to assess the friability of tablets. We took twenty tablets and weighed them. The tablets were weighed before being put in the Roche friability, which uses a plastic chamber that rotates at 25 RPM/100 rotations and drops the tablets six inches each time to combine the effects of shock and abrasion. The tablets were taken out and weighed again after the procedure.

Friability is ascertained by

$$F=100(1-W_o/W_t)$$

## RESULTS AND DISCUSSION

### Preformulation study

#### Drug excipient interaction/ Compatibility study

#### DISCUSSION:

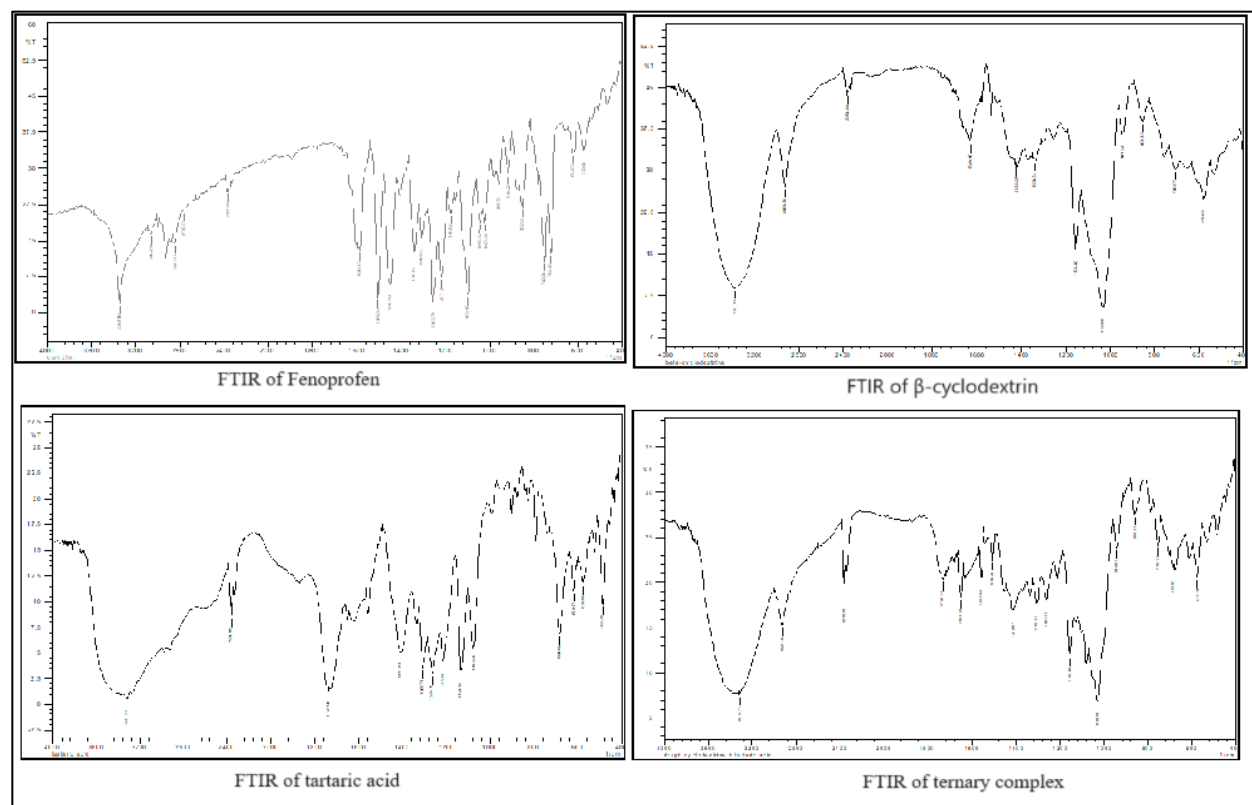
Pre-compressional micrometric parameters (derived and flow properties) were assessed for the manufactured powder blends of all fifteen formulations. A key component in the creation of solid doses and process development is bulk density. For example, it's employed to figure out how much powder can fit into a hopper on a tablet press or blender. The bulk densities of all the

developed formulations ranged from 0.51 to 0.56 gm/cc. A popular statistic for describing powders is the tapped density, which is quick and straightforward to measure. How well a powder sample packs under taps measures its cohesiveness, which is connected to its flow ability.

Post-compressional parameters such as hardness, friability, weight variation, thickness, in-vitro dispersion time, wetting time, water absorption ratio, and drug concentration were evaluated for the prepared tablets. The hardness of the tablets was found to vary from  $2.3 \pm 0.19$  to  $2.9 \pm 0.13$  kg/cm<sup>2</sup>. It was found that every tablet was strong enough to withstand handling and storage conditions without cracking. All of the pills demonstrated acceptable friability by the certified

**Table 1 FTIR data of drug and Polymer Mixtures**

Observations	Fenoprofen	$\beta$ -cyclodextrin	Tartaric acid	Ternary complex
O-H stretching	3050	2924	3321	3315
C=O stretching	1589	1028	1737	1782
C-C stretching	1255	1305	1265	1261
C-O stretching (R-O-R)	1176	1028	1134	1305
C-H stretching	2830	2924	1255	2924



**Figure 2 FTIR Spectrums of drug and Polymer Mixtures**

pharmacopeia, with no tested batch having a percentage friability greater than 1%. The percentage of friability for each batch was found to range from 0.38 to 0.86%, indicating good mechanical resistance for the tablets. Thus, tablets could withstand pressure and mechanical shocks during handling, shipping, storage, and production operations.

Drug-excipient interactions are essential for the drug's release from the formulation, among other factors. FTIR techniques have been employed to investigate the chemical and physical interactions between the drug and the excipient.

The FTIR spectra of pure drug,  $\beta$ -cyclodextrin, tartaric acid, and complex are shown in Figure --- No significant changes in the FTIR spectra of the complex were observed. The broadening of the peak was probably due to the restriction of bending and stretching vibration of the molecule due to the cyclodextrin cavity.

The Figure exhibited the FTIR spectrum of fenoprofen, their characteristic peak, and their interpretation, which is given in Table No. The distinctive peak of ether, C-O stretching of alcohol, and carbonyl compound is the significant peak confirming the identity of fenoprofen. Respectively. Shifting in the peak of O.H. and carbonyl group indicates the physical interaction of the respective compound, and the appearance of characteristics peak depicted that no chemical changes were observed in the respective drug and another compound it indicated that changes in the solubility behavior occurred only due to the physical interaction between the molecule.

## CONCLUSION

The transdermal route has gained accolades as it has several advantages over conventional forms. Oral routes of drug administration have wide acceptance. Solid dosage forms, like tablets and capsules, are accessible for administration, pain avoidance, accurate dosage, and self-medication. A critical drawback of this dosage form is that patients often experience difficulty swallowing. Approximately one-third of the population have a geriatric and pediatric problem, and Patients on chemotherapy treatment have swallowing difficulties, which leads to reduced overall therapy effectiveness.

Fast-dissolving tablets (FDTs) have recently been the most demanding concept based on requests from patients to enhance their quality of life. Water is unnecessary for the fast-dissolving tablets to dissolve quickly in the saliva. Drugs may enter systematic circulation by directly passing via the oral mucosa, avoiding the gastrointestinal tract and first passing through the liver's processing. A fast-dissolving tablet has been designed to provide convenience in dosing without water and ease of use together.

The present invention relates to a fast-dissolving tablet with a pharmacologically active ingredient a vitamin, an antipyretic-analgesic-anti-inflammatory agent, an antihypertensive drug, a psychotropic drug, an antidiabetic drug, or something similar—and a carbohydrate. The tablet should have sufficient strength and dissolve and disintegrate quickly in the oral cavity. Additionally, the method of making the tablet has been described. The main aim of the proposed project is to develop a mouth-dissolving tablet for fenoprofen's taste masking. Fenoprofen is a potent NSAID agent that can improve gastric irritation. It has moderate bioavailability and is highly bitter.

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