Solubility Enhancement of Poorly Water Soluble Drug by Using Nanoparticles Approach

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➢ *Abstract:*

Drugs that are poorly soluble in water can be formulated with nanoparticles to increase their Solubility. To improve solubility and bioavailability, the main goal of the current study was to create and assess fenofibrate-loaded nanoparticles using the Emulsification Solvent Evaporation method. The Emulsification Solvent Evaporation method was used to create nanoparticles of the BCS class II medication fenofibrate, which were then characterized by in vitro drug release studies, scanning electron microscopy, powder X-ray diffraction, Fourier-transform infrared spectroscopy, and zeta potential. Data from Fourier-transform infrared spectroscopy, revealed no interactions between the drug and the polymers. Nanoparticles were shown to be spherical in shape using scanning electron microscope pictures. When compared to the pure drug, the water solubility of drug-loaded nanoparticles rose and their dissolving profile improved, demonstrating the ease and accuracy of nanoprecipitation. The solubility and bioavailability of BCS class II medications could be improved by using this laboratory-scale method and this strategy. [1]

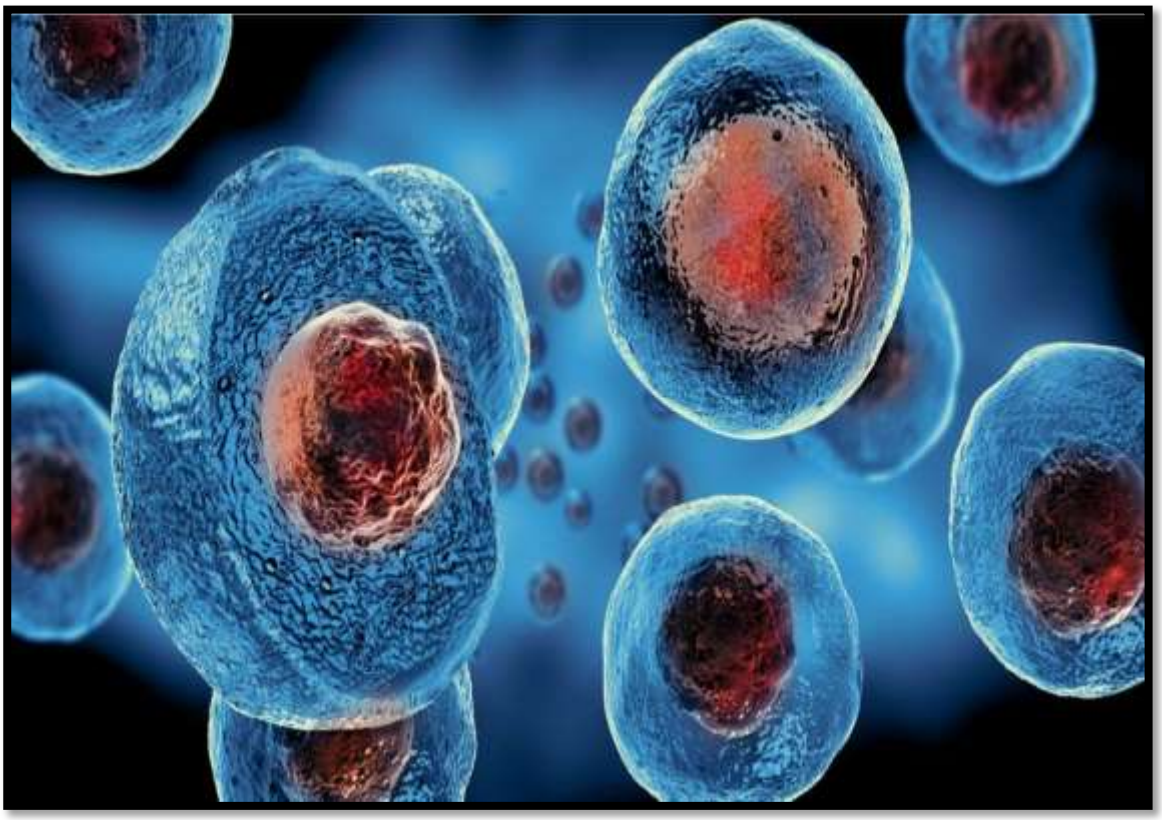
➢ Keywords:

Fenofibrate, BCS class 2, nanoparticles, emulsification solvent evaporation method, evaluation parameters, dosage form capsule.

➢ Introduction:

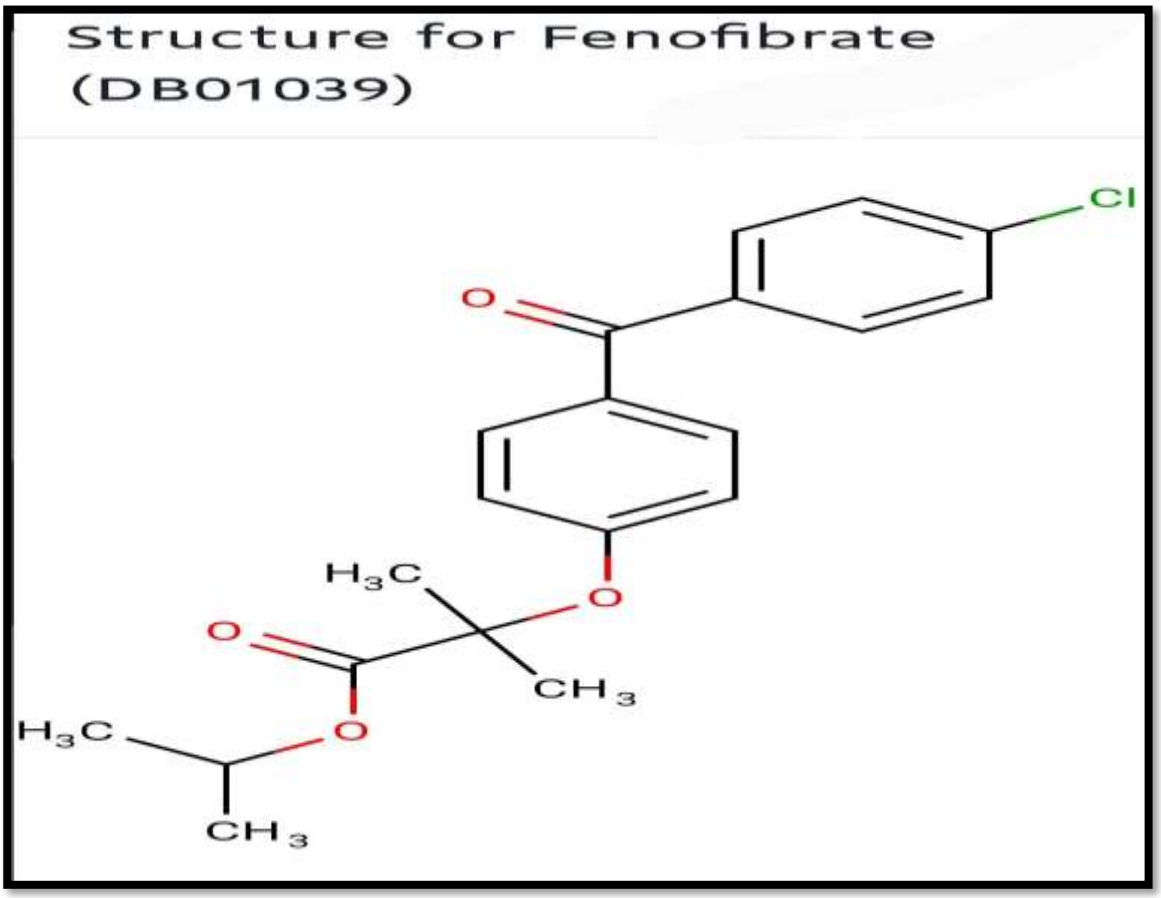
Absorption, distribution, metabolism, and excretion are the four fundamental mechanisms of drug transport and modification in the body that affect a medicine's therapeutic efficacy. Numerous reasons can contribute to therapy failure, including insufficient drug concentration due to poor absorption, substantial swings in plasma levels due to uncertain bioavailability, quick metabolism and excretion, and poor drug solubility [2] One workable solution to these problems is to design a suitable medication colloidal carrier system.

Colloidal particles of a size range of 10–1000 nm are called nanoparticles, and they include dissolved or trapped active ingredients, such as drugs or physiologically active materials [3]. Polymeric micelles, solid-lipid nanoparticles, dendrimers, liposomes, Nanospheres, and Nanocapsules are among the several kinds of these. according to advancements in nanotechnology, drug nanoparticles that can be used in a number of creative ways can now be produced. It is now possible to use new drug delivery methods to improve medication efficacy and lessen adverse effects [4]



Nanoparticles[5]

For a medicine to exhibit good bioavailability and consequently, therapeutic impact, solubility is the most crucial factor [6,7] Poor water solubility affects almost 40% of novel pharmacological entities, which usually makes it difficult to formulate them into traditional dosage forms and reduces their bioavailability [8]. Fenofibrate is a peroxisome proliferator receptor alpha activator used to lower LDL-C, total -C, triglycerides, and Apo B, while increasing HDL-C in hypercholesterolemia, dyslipidemia, and hypertriglyceridemia. Fenofibrate is a fibric acid derivative like clofibrate and gemfibrozil. [9] Fenofibrate is used to treat primary hypercholesterolemia, mixed dyslipidemia, severe hypertriglyceridemia. [10,11] Fenofibrate was granted FDA approval on 31 December 1993. [12]



Structure [13]

- **Materials and Methods:**
- **Materials:**

Material	Source of Material
Fenofibrate	Amepurva forum Nirant Institute Of Pharmacy
HPMC	LOBA CHEMIE PVT.LTD
Ethyl acetate	LOBA CHEMIE PVT.LTD
Tween 80	LOBA CHEMIE PVT.LTD
Distilled Water	-

- **Method:** [14]

Nanoparticles prepared by emulsification solvent evaporation method. This method contains mainly three step.

- First step -is preparation of organic phase,
- second is preparation of aqueous phase,

- Third phase is drop wise addition of organic phase into aqueous phase with continue magnetic stirrer for 20 min.

➢ Formulation Table: -

Sr. No.	Drug (gm)	HPMC(gm)	Ethyl acetate (ml)	Tween 80 (ml)	Distilled water (ml)
F1	0.5 gm	0.5 gm	5 ml	1.5 ml	7 ml
F2	0.5 gm	1 gm	2.5 ml	2.5 ml	5 ml
F3	1 gm	2 gm	5 ml	3 ml	10 ml
F4	4 gm	8 gm	20 ml	12 ml	40 ml
F5	4 gm	8 gm	20 ml	12 ml	40 ml

1] **First step:** -

To prepare the **first phase**, add polymer & Drug is dissolved in suitable organic solvent (in which drug is very soluble).and magnetic stirrer for 5 min. And that solvent must be water miscible. If drug have low solubility then apply the external force to it by providing sonication, sonicate the organic phase for 10-15 min.

Fig. 1: - Organic Phase

2] **Second step: -**

In **second phase** water is mixed with surfactant stabilizers & properly mixed with continue stir for 5 min.

Fig. 2: - Aqueous Phase

3] **Third step: -**

The **third phase** have dropwise addition of organic phase into aqueous phase, continuous stirring on the magnetic stirrer at 1500 rpm, like that way the nanoparticles was prepared. these Nanoparticle solid form evaporate the organic solvent at some using magnetic stirrer at 350rpm then centrifuge at 1000 to 1500 rpm for 5 to 10 min and wash with water or ethanol and filter Kept the sample 24hr in Desiccator and dried, and collect the Nanoparticle and stored.

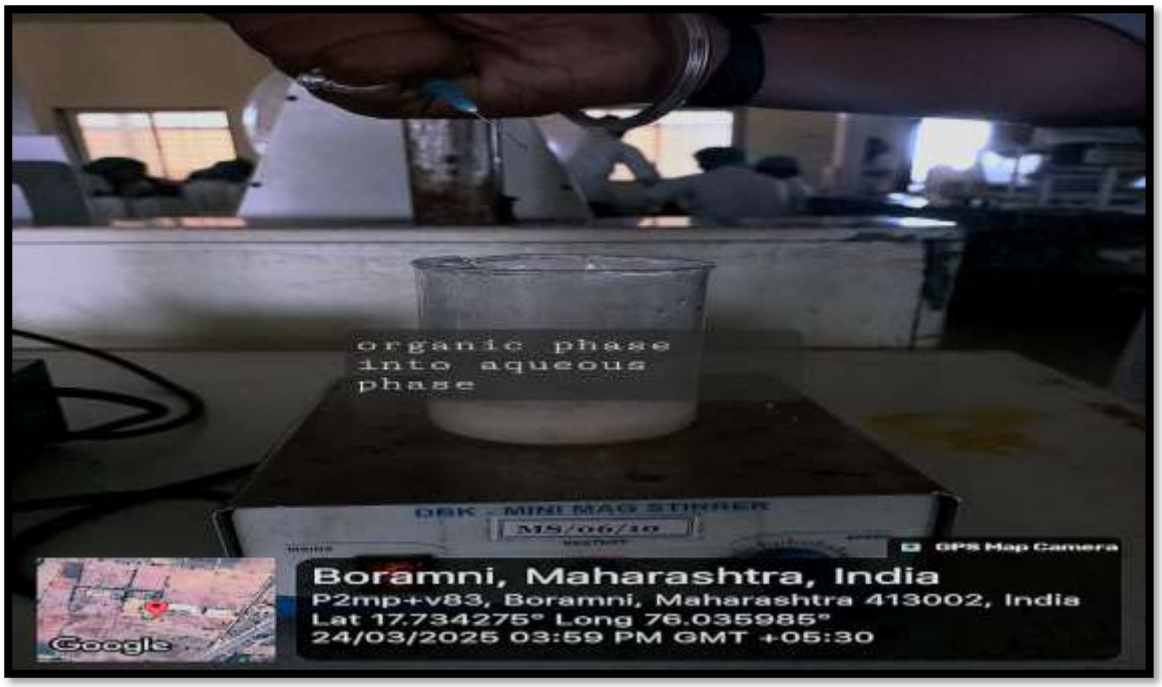


Fig. 3: - Addition of Organic phase into aqueous phase

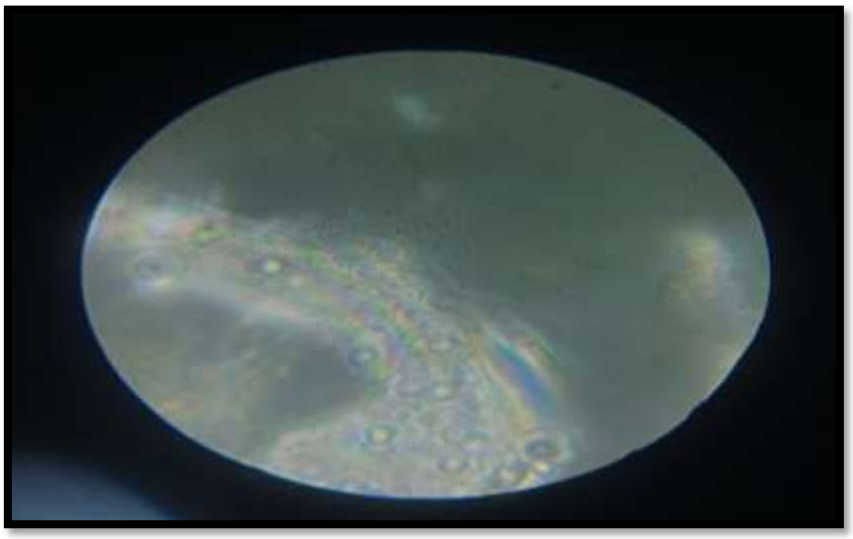
Fig. 4: - Centrifugation of nanoparticle suspension

Fig 5: - Filtration and collection of nanoparticles

- **Evaluation Test of fenofibrate Nanoparticles: -**

1] **Microscopic Evaluation:** -

For microscopical evaluation, we have used a compound microscope of power 100x, which gives us a magnification range where the nanoparticle range is about 1nm to 100nm.



Fig, 6: - Microscopic image of nanoparticles

2] Solubility test: -

Prepared Fenofibrate nanoparticles by dissolving 10-50 mg in 10 ml of water and Ethanol. The solution is shaken at 150 rpm for 24 hours at room temperature to Ensure equilibrium. Shaking continues for a few more hours to allow undissolved Particles to settle for 1-2 hours. The solution is filtered Whatman filter paper, and The clear filtrate is transferred to a beaker. The solvent is removed using a water Bath at 50-60°C, and the remaining solid is weighed after evaporation. And Calculate the solubility using formula :

$$\text{Solubility \% :} \quad \frac{\text{Mass of Dissolved fenofibrate nanoparticle(mg)}}{\text{Volume of solvent (ml)}}$$

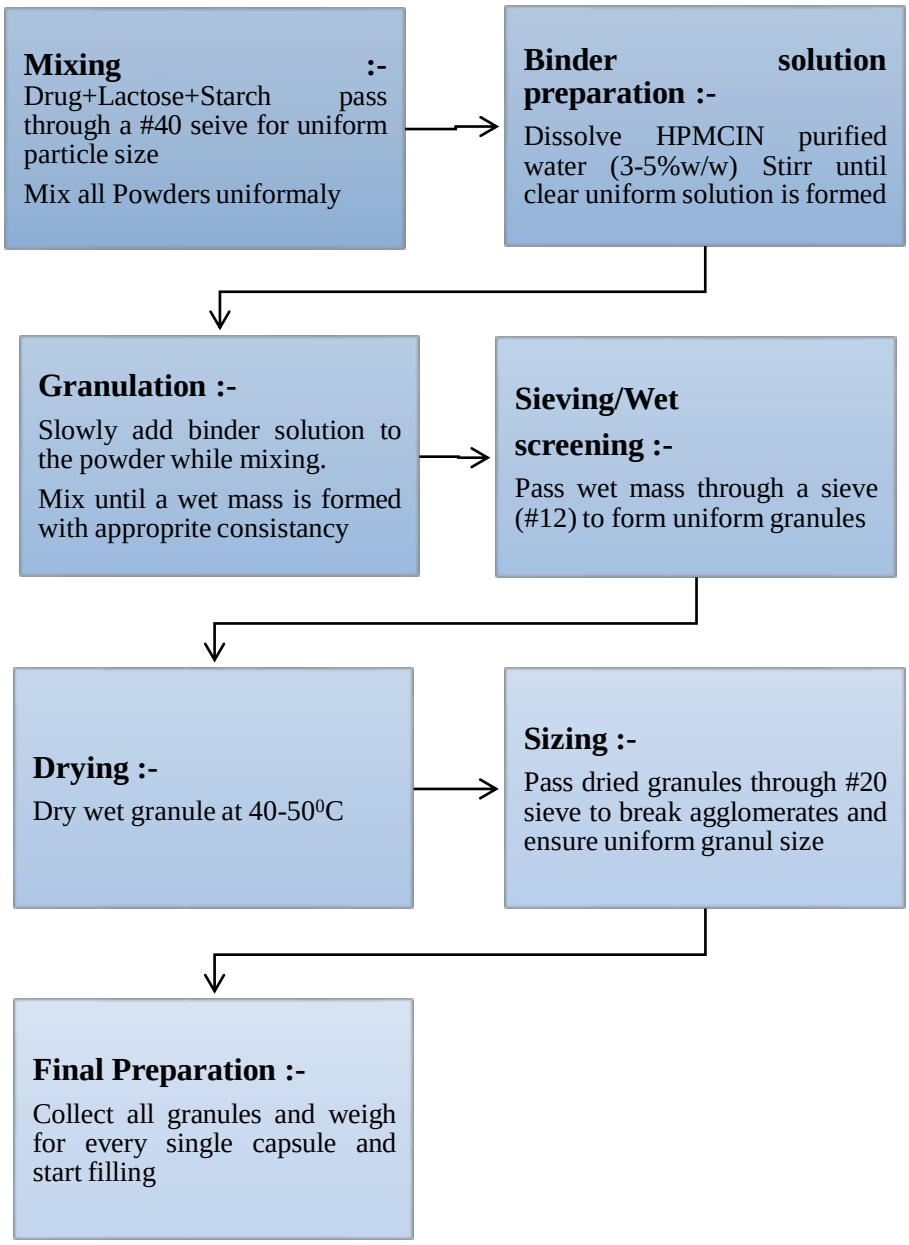
3] Drug Content: -

The drug content of the prepared Fenofibrate nanoparticles was determined using UV-Visible spectrophotometry. Take a known valume of nanoparticle and add in appropriate solvent (methanol) and sonicated to ensure complete solubilization. filter and Analyze at wavelength Range 200nm to 400 nm and check absorbance at 290 nm. The drug content was found to be in the range of 95% to 99%, indicating efficient drug loading in the nanoparticulate formulation

- **Preparation of Fenofibrate Nanoparticles Capsule :-**
- **Material And Method :-**

Sr. No.	Material	Role
1	Fenofibrate Nanoparticles	Drug
2	Lactose	Filler/diluent
3	Starch	Disintegrant
4	HPMC (3-5%)	Binder (In Solution)
5	Water	-

- **Method :-**
- **Granulation Process :-**



- **Formulation of capsule containing Fenofibrate Nanoparticle: -**

Take the prepared dry NPs and excipient like filler, Disintegration, Binder etc. Weight the all ingredient properly &Mix the all ingredients using mortar & pestle. Then prepare the granules and dry Afterwards pass that mixture from sieve no 80& fill it in capsule.

Fig. 7: - Fenofibrate Nanoparticle Capsules

- **Evaluation test of fenofibrate nanoparticle Capsules: -**

1.weight variation test: -

Twenty capsules are weighed separately using an analytical balance to perform the weight variation test. The average mass is then determined and compared to the mass of each individual pill. Each capsule should weigh no more than ±7.5% of the average. Weigh the 20 capsules again, being careful to maintain each one's identification, and totally empty the contents if none of them fall within these ranges.

Fig.8: - Weighing capsule individual

3.Disintegration: -

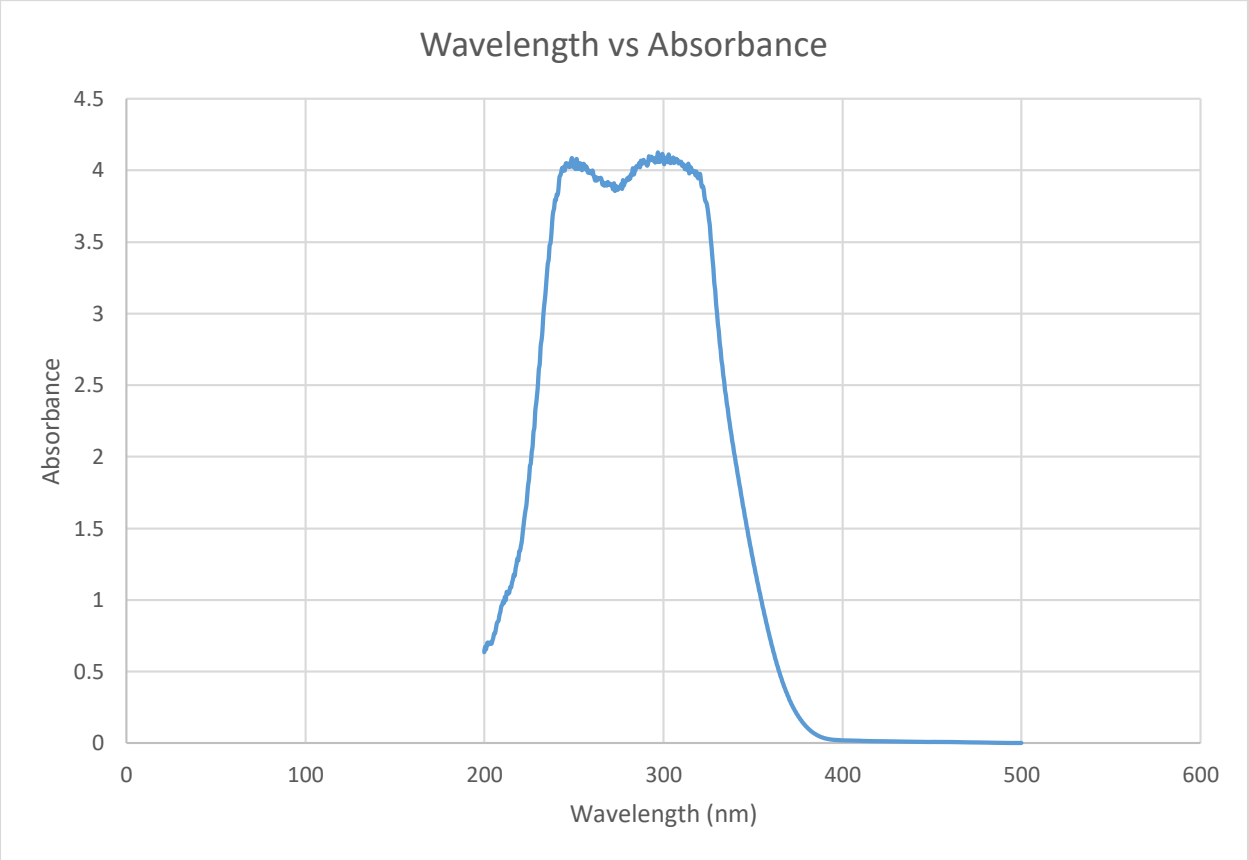
A basket that can hold one to six capsules is used to conduct a disintegration test for capsules. The stomach's 37°C temperatures are then replicated by raising and lowering this into a beaker of water. The tablets or capsules are covered with perforated plastic discs to keep them under the surface if they float.

Fig.9: - Disintegration test

Level of the water. When there is no residue in the mesh, the capsule disintegration time is measured.

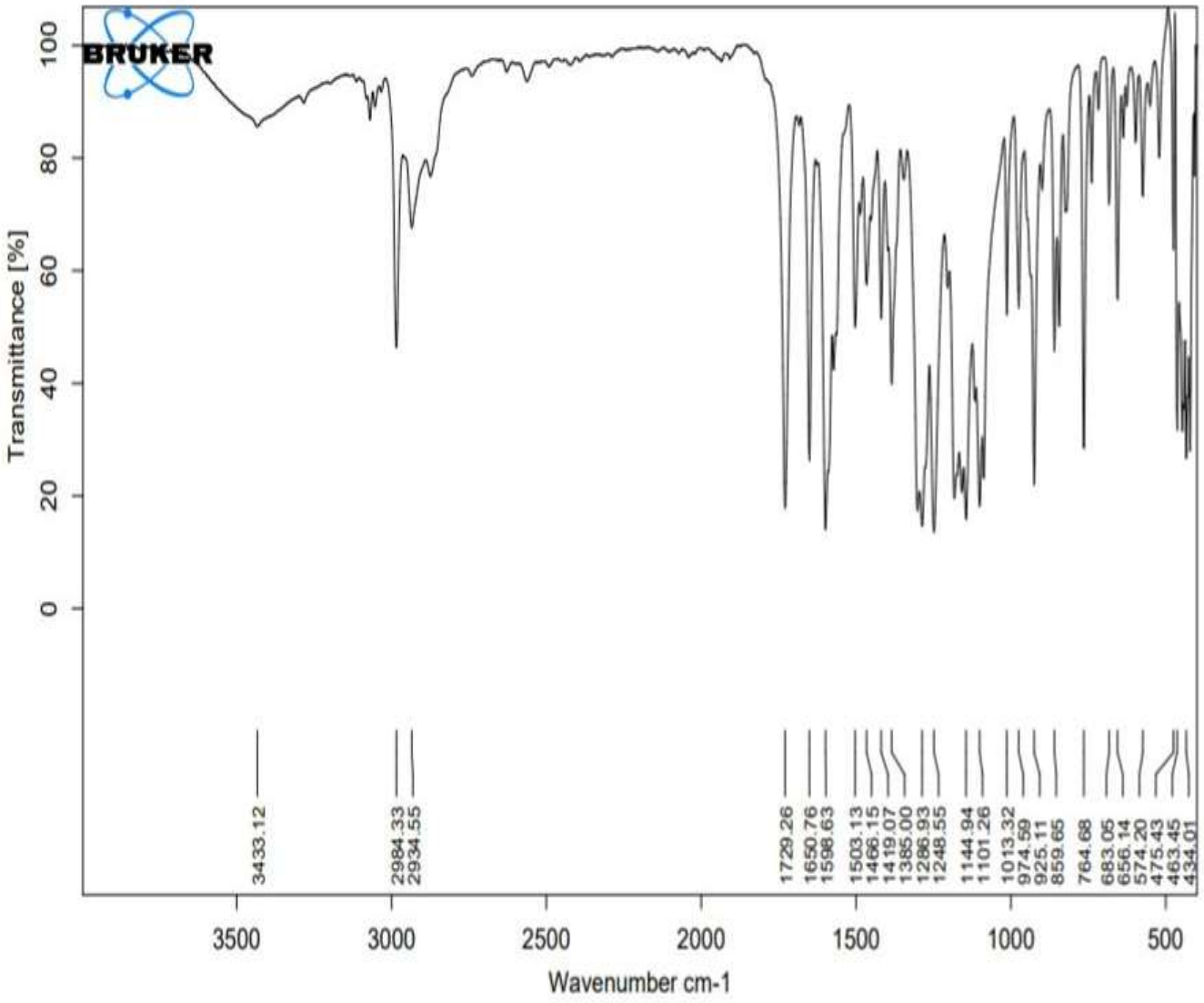
- **Result: -**
- **Preformulation Evaluation: -**

1] UV spectroscopy: -



Graph 1: - UV spectroscopy of Fenofibrate nanoparticles

1.FTIR of Fenofibrate:



Graph 2: - Systematic Representation of FTIR of Fenofibrate

2.Table: Interpretation of FTIR of Fenofibrate; -

Sr.No	Reported range	Observed range	Functional groups
1.	3500-3200	3433.12	O-H stretch (Alcohol) or N -H (Amine)
2.	3000-2840	2984.33 2934.55	C-H stretch (SP^3) (Alkene)
3.	1750-1680	1729.26	C=O stretch
4.	1600-1450	1650.76 1598.63 1503.13 1466.15 1419.07 1385.00	C=C stretch or Amide Linkage
5.	1300-1000	1286.93 1248.55 1144.94 1101.26	C-O stretch (Ether / Ester)
6.	900-650	859.65 764.68 683.05 656.14	C-H blend (Aromatic)
7.	850-500	574.20 475.43 463.45 434.01	C-X stretch (Halide)

2.weight variation:

Capsule no.	Weight of individual capsule
1	0.35
2	0.36
3	0.35
4	0.36
5	0.34
6	0.36
7	0.35
8	0.35
9	0.37
10	0.35
11	0.34
12	0.35
13	0.35
14	0.35
15	0.35
16	0.34
17	0.35
18	0.34
19	0.35
20	0.35

3.Disintegration test:

Name of Instrument	Batch	Disintegration Time
D.T. Apparatus Electrolab	1	26.20
D.T. Apparatus Electrolab	2	29.02

- **Reference:**

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