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Research Article

DRUG EXCIPIENT COMAPATIBILITY STUDIES FOR MESALAMINE NANOSPEHERE FORMULATION

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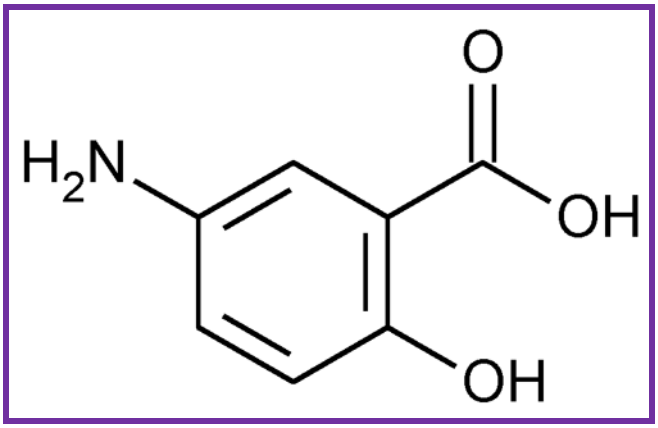
Abstract:
Drug and excipient compatibility is first step of pre-formulation studies for choose the best excipient for better and suitable formulation, this research article proposed that by the use of FT-IR checked the compatibility of drug with excipients, and finally concluded that that there was no significant Drug- Excipients interaction was observed. The results of FTIR study shown that there is no change in drug's melting peak after the preparation of tablet. So we can conclude that drug and other excipients are compatible which each other.
Key words: Nanospheres, Mesalamine, FT-IR, Compatibilities, Eudragit R and S.

INTRODUCTION

The powder of Mesalamine and KBr were prepared using hydraulic pellet press at a pressure of 7 to 10 tones. FTIR was scanned from 400-4000cm-1 by using perkin Elmer spectrum GX FTIR. FTIIR study was carried out individually for drug, each polymer and finished product (tablet) compared Aspirin FTIR spectra of pure drug and polymer.

The Infra-Red absorption spectrum of the finely ground sample in KBr dispersion compressed into a disc should exhibit maxima only at the same wavelengths as that of a similar preparation of working standard.



Class: Anti-inflammatory Agents
Chemical Name: 5-Amino-2-hydroxybenzoic acid
Molecular Formula: $C_7H_7NO_3$
Molecular Weight: 153.135 g/mol
Melting Point: 283°C
Solubility:
Slightly soluble in Water (0.84 g/L at 20°C) and alcohol; more soluble in hot Water soluble in hydrocloric acid. Insoluble in ethanol
Log P: 1.2
Route of administration: Oral, Rectal
Dose:
375 mg extended release capsules: 1.5 g (4 capsules) orally once a day.
400 and 800 mg tablets and capsules: 1.6 g orally daily in divided doses.
1200 mg tablets: 2.4 g (2 tablets) orally once a day with food.
Brands: Asacol, Canasa, Lialda, Pentasa, Rowasa
Bioavalibility:
Following oral administration of 400 mg delayed release tablet (Asacol) Approximately 28% of mesalamine is absorbed and the remaining of the dose is available for topical and activity and fecal excreation.
Following oral administration of extand release capsule (Pentasa) about 20-30% of the drug is absorbed.
Following oral administration of 1-2 gm delayed release tablet (Lialda) about 21-22% of the drug is absorbed.
Mechanism of action:
Mucosal production of arachidonic acid metabolites, both through the cyclooxygenase and lipoxygenase pathways, is increased in patients with inflammatory bowel disease. Mesalamine appears to diminish

inflammation by inhibiting cyclooxygenase and lipoxygenase, thereby decreasing the production of prostaglandins, and leukotrienes and hydroxyeicosatetraenoic acids (HETs), respectively. Following rectal or oral administration, only a small amount of mesalamine is absorbed; the remainder, acting topically, reduces bowel inflammation, diarrhea, rectal bleeding and stomach pain.

Absorption:

20 to 30% absorbed following oral administration. 10 to 35% absorbed from the colon (rectal suppository) - extent of absorption is determined by the length of time the drug is retained in the colon.

Plasma Protein Binding:

Approximately 44-55% (as unchanged drug).

Approximately 43% at concentration of 2.5 mcg/ml.

Metabolism:

Metabolised in liver to form N-Acetyle 5-aminosalicylic acid.

Excreation:

Following oral administration 20% excreted in urine as metabolise and faces.

Following rectal administration 50% excreted in faces as unchanged drug and metabolite and 10-35% in urine

Half life:

400 mg delayed release tablet (Asacol) 12 hour (2-15 hours).

1.2 gm delayed tablet (lialda) 7-9- hours.

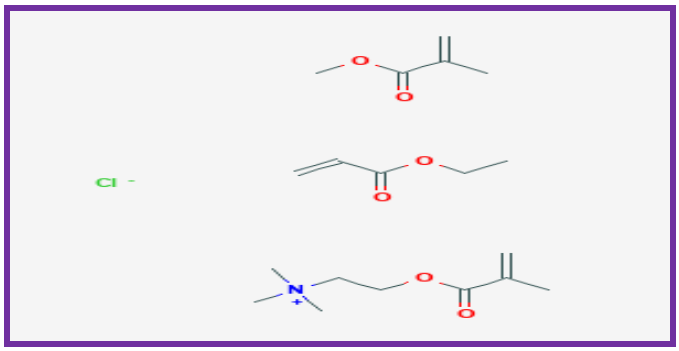
Rectal suppositories 0.5-1.5 hours.

Storage:

20-25^{0}C

Uses:

Mesalazine (INN, BAN), also known as Mesalamine (USAN) or 5-aminosalicylic acid (5-ASA), is an anti-inflammatory drug used to treat inflammation of the digestive tract (Crohn's disease) and mild to moderate ulcerative colitis. Mesalazine is a bowel-specific aminosalicylate drug that is metabolized in the gut and has its predominant actions there.



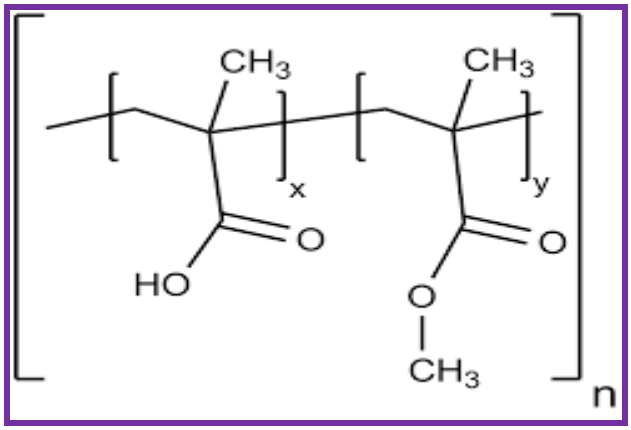
Molecular Formula: $C_{19}H_{34}ClNO_6$

Chemical Names: Eudragit RS
ethyl prop-2-enoate; methyl 2-methylprop-2-enoate; trimethyl-[2-(2-methylprop-2-enoyloxy)ethyl]azanium; chloride
UNII-8GQS4E66YY
UNII-161H3B14U2
33434-24-1

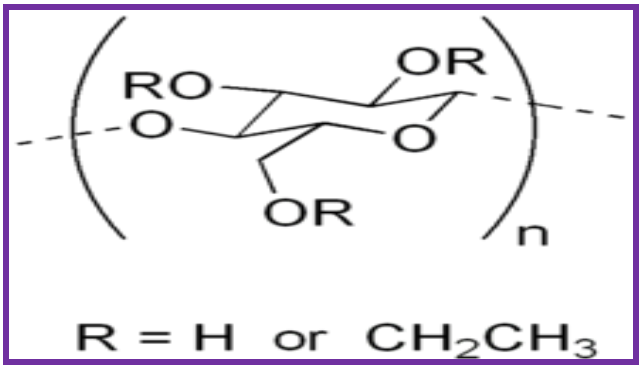
Molecular Weight: 407.9 g/mol

3.2.2. Eudragit L

Eudragit L contains an anionic copolymer based on methacrylic acid and ethyl acrylate. Physical properties: It is a solid substance in form of a white powder with a faint characteristic odour.



3.2.3. Ethyl cellulose



Nonproprietary Names

BP: Ethylcellulose

PhEur: Ethylcellulosum

USPNF: Ethylcellulose

Synonyms: Aquacoat ECD; Aqualon; E462; Ethocel; Surelease.

Chemical Name: Cellulose ethyl ether

Empirical Formula and Molecular Weight: Ethylcellulose with complete ethoxyl substitution (DS = 3) is $C_{12}H_{23}O_6(C_{12}H_{22}O_5)nC_{12}H_{23}O_5$ where n can vary to provide a wide variety of molecular weights. Ethylcellulose, an ethyl ether of cellulose, is a long-chain polymer of b-anhydroglucose units joined together by acetal linkages.

Functional Category: Coating agent, Flavoring fixative, Tablet binder, Tablet filler, Viscosity increasing agent.

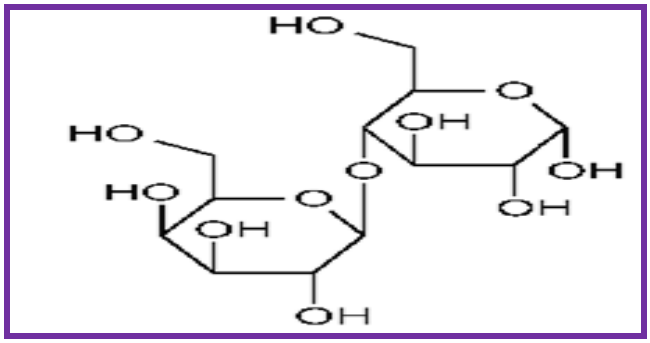
Applications in Pharmaceutical Formulation or Technology

Ethylcellulose is widely used in oral and topical pharmaceutical formulations. The main use of ethylcellulose in oral formulations is as a hydrophobic coating agent for tablets and granules. (1-8) Ethylcellulose coatings are used to modify the release of a drug, (7–10) to mask an unpleasant taste, or to improve the stability of a formulation; for example, where granules are coated with ethylcellulose to inhibit oxidation. Modifiedrelease tablet formulations may also be produced using ethylcellulose as a matrix former.

Description: Ethylcellulose is a tasteless, free-flowing, and white to light tan colored powder.

Stability and Storage Conditions: Ethylcellulose is a stable, slightly hygroscopic material. It is chemically resistant to alkalis, both dilute and concentrated, and to salt solutions, although it is more sensitive to acidic materials than are cellulose esters. Ethylcellulose is subject to oxidative degradation in the presence of sunlight or UV light at elevated temperatures. This may be prevented by the use of antioxidant and chemical additives that absorb light in the 230–340nm range. Ethylcellulose should be stored at a temperature not exceeding 32^0C (90^0F) in a dry area away from all sources of heat.

3.2.4 Lactose Anhydrous



Nonproprietary Names:

- BP: Anhydrous lactose
- JP: Anhydrous lactose
- PhEur: Lactosum anhydricum
- USPNF: Anhydrous lactose

Synonyms: Anhydrous Lactose NF 60M; Anhydrous Lactose NF Direct Tableting; Lactopress Anhydrous; lactosum; lattioso; milk sugar; Pharmatose DCL 21; Pharmatose DCL 22; saccharum lactis; Super-Tab Anhydrous

Chemical name: *O*-β-D-galactopyranosyl-(1→3)-β-D-glucopyranose

Empirical formula: $C_{12}H_{22}O_{11}$

Molecular weight: 332.30 gram/ mol

Functional category: Binding agent; directly compressible tableting excipient; lyophilization aid; tablet and capsule filler.

Description: Lactose occurs as white to off-white crystalline particles or powder. Several different brands of anhydrous lactose are commercially available which contain anhydrous β-lactose and anhydrous α-lactose.

Applications in Pharmaceutical Formulation or Technology: Anhydrous lactose is widely used in direct compression tableting applications and as a tablet and capsule filler and binder.

Melting Point:

- 223.0°C for anhydrous α-lactose;
- 252.2°C for anhydrous β-lactose;
- 232.0°C (typical) for commercial anhydrous lactose

Water Content:

Loss on drying ≤0.5% and ≤1.0% water content for Anhydrous Lactose NF Direct Tableting and

Solubility: Soluble in water; sparingly soluble in ethanol (95%) and ether

Stability and storage condition:

Lactose may develop a brown coloration on storage, the reaction being accelerated by warm, damp conditions; At 80°C and 80% RH, tablets containing anhydrous lactose have been shown to expand 1.2 times after one day.

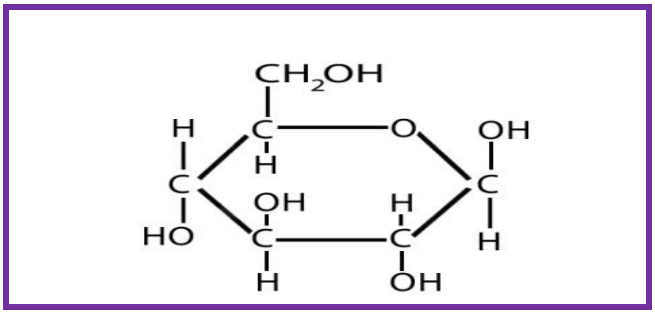
Incompatibilities:

Lactose anhydrous is incompatible with strong oxidizers. When mixtures containing a hydrophobic leukotriene antagonist and anhydrous lactose or lactose monohydrate were stored for six weeks at 30°C and 75% RH, the mixture containing anhydrous lactose showed greater moisture uptake and drug degradation.

Safety:

The Lactose is widely used in pharmaceutical formulations as a diluent and filler-binder in oral capsule and tablet formulations. It may also be used in intravenous injections.

3.2.5 Dextrose



Nonproprietary Names

BP: Glucose

JP: Glucose

PhEur: Glucose Monohydrate

USP: Dextrose

Synonyms: Blood sugar; Caridex; corn sugar; C*PharmDex; Dextrofin; D-(þ)- glucopyranose monohydrate; glucosum monohydricum; grape sugar; Lycadex PF; Roferose; starch sugar; Tabfine D-100.

Chemical Name: D-(þ)-Glucose monohydrate

Empirical Formula: $C_6H_{12}O_6.H_2O$

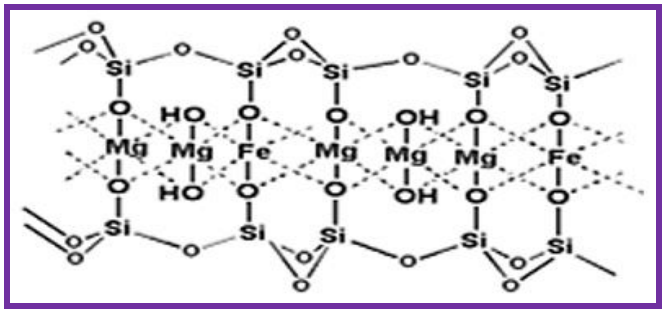
Molecular Weight: 198.17 gram/ mol

Functional Category: Tablet and Capsule diluents, Therapeutic agent, Tonicity agent, sweetening agent.

Applications in Pharmaceutical Formulation or Technology: Dextrose is widely used in solutions to adjust tonicity and as a sweetening agent. Dextrose is also used as a wet granulation diluents and binder, and as a direct-compression tablet diluent and binder, primarily in chewable tablets. Although dextrose is comparable as a tablet diluent to lactose, tablets produced with dextrose monohydrate require more lubrication, are less friable, and have a tendency to harden.(1–3) The mildly reducing properties of dextrose may be used when tableting to improve the stability of active materials that are sensitive to oxidation. Dextrose is also used therapeutically and is the preferred source of carbohydrate in parenteral nutrition regimens.

Description: Dextrose occurs as odorless, sweet-tasting, colorless crystals or as a white crystalline or granular powder.

3.2.6 Talc



Synonyms: Hydrous magnesium calcium silicate.

Chemical Name: Talc.

Empirical Formula: Approximate $Mg_6(Si_2O_5)_4(OH)_4$

Functional Category:

Anticaking agent; glidant; tablet and capsule diluent; tablet and capsule lubricant.

Application in Pharmaceutical Formulation

Table: 3.1 Uses of Purified Talc

Use	Concentration (%)
Dusting powder	90.0–99.0
Glidant and tablet lubricant	1.0–10.0
Tablet and capsule diluents	5.0–30.0

Talc is used as a lubricant in tablet formulations; in a novel powder coating for extended-release pellets; and as an adsorbent. In topical preparations, talc is used as a dusting powder, although it should not be used to dust surgical gloves. Talc is a natural material; it may therefore frequently contain microorganisms and should be sterilized when used as a dusting powder. Talc is additionally used to clarify liquids and is also used in cosmetics and food products, mainly for its lubricant properties.

Description:

Talc is very fine, white to grayish white, odorless, impalpable, crystalline powder. It adheres readily to skin and soft to touch and free from grittiness.

pH: 7-9.

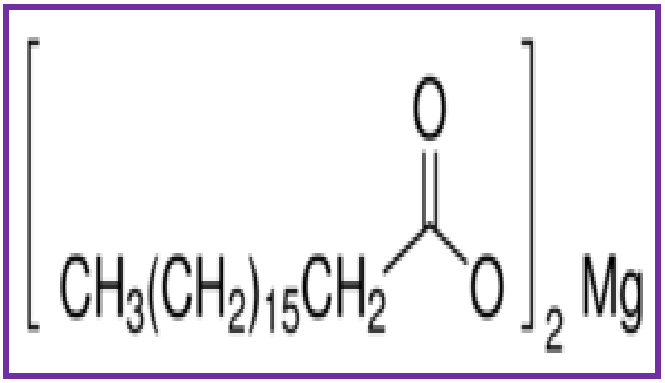
Solubility: Practically insoluble in dilute acids and alkalis, organic solvents, and water.

Stability and Storage:

Talc is a stable material and may be sterilized by heating at 160°C for not less than 1 h. It may also be sterilized by exposure to ethylene oxide or gamma irradiation. Talc should be stored in a well-closed container in a cool, dry place.

Incompatibility: It is incompatible with quaternary ammonium compounds.

3.2 7. Magnesium stearate[27]



Synonyms: Magnesium octadecanoate, Octadecanoic acid, Stearic acid.

Empirical Formula: $C_{36}H_{70}MgO_4$;

Molecular Weight: 591.34.

Application in Pharmaceutical Formulation:

Primarily used as lubricant in capsule and tablet at a concentration between 0.25%-5.0% w /w.

Description:

Magnesium stearate is very fine, light white, precipitated or milled impalpable powder of low bulk density having a faint order of stearic acid and characteristic taste. Capsule dissolution is also sensitive to both the amount of magnesium stearate in the formulation and the mixing time; higher levels of magnesium stearate and long mixing times can result in the formation of hydrophobic powder beds that do not disperse after the capsule shell dissolves.

An increase in the coefficient of variation of mixing and a decrease in the dissolution rate have been observed following blending of magnesium stearate with a tablet granulation. Tablet dissolution rate and crushing strength decreased as the time of blending increased; and magnesium stearate may also increase tablet friability. Blending times with magnesium stearate should therefore be carefully controlled.

Loss on Drying: ≤6.0%.

Solubility: Practically insoluble in ethanol (95%), ether and water; slightly soluble in warm benzene and warm ethanol (95%).

Incompatibility:

Incompatible with strong acids, alkalis and iron salts. Avoid mixing with strong oxidizing materials. Magnesium stearate cannot be used in product containing aspirin, some vitamins and most alkaloidal salts.

EXPERIMENTAL WORK:

The powder of Mesalamine and KBr were prepared using hydraulic pellet press at a pressure of 7 to 10 tones. FTIR was scanned from 400-4000cm-1 by using perkin Elmer spectrum GX FTIR. FTIIR study was carried out individually for drug, each polymer and finished product (tablet) compared Aspirin FTIR spectra of pure drug and polymer.

The Infra-Red absorption spectrum of the finely ground sample in KBr dispersion compressed into a disc should exhibit maxima only at the same wavelengths as that of a similar preparation of working standard.

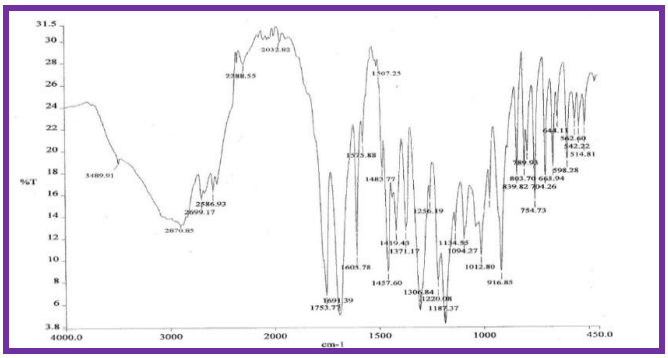


Figure 7.1: IR spectrum of Mesalamine

Table 7.2: Wave number of functional groups of Mesalamine

Sr. No.	Wave number	Functional group
1	1600-1400 cm^{-1}	C=C (Aromatic)
2	1750-1730 cm^{-1}	C=O (ester)
3	1725-1700 cm^{-1}	C=O (carboxylic acid)
4	1300-1000 cm^{-1}	C-O (ester/carboxylic acid)
5	3300-2500 cm^{-1}	O-H (carboxylic acids)

The above peaks can be considered as characteristic peaks of Mesalamine

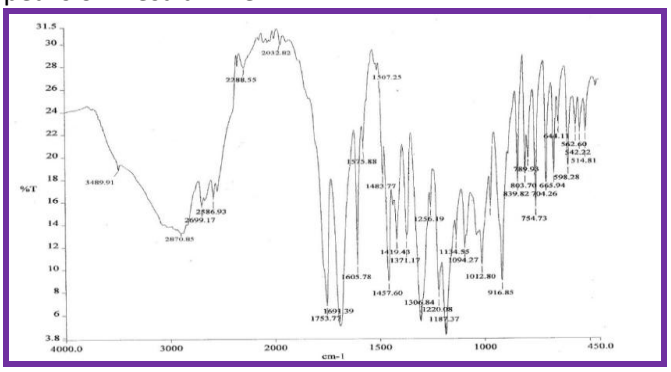


Fig.7.5 FTIR Analysis result of Mesalamine

7.2.1.2 FTIR Analysis result of Drug + HPMC 6cps **FTIR Analysis result of Drug + HPMC 6cps**

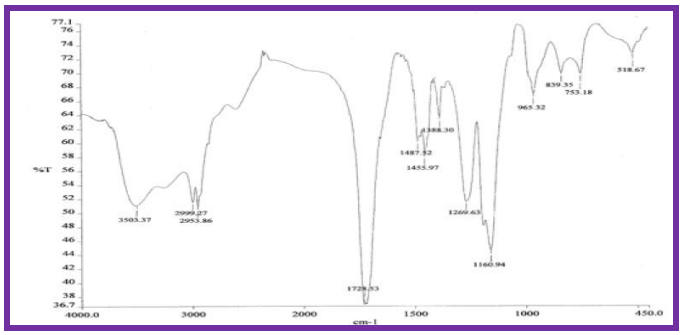


Fig.7.6 FTIR Analysis result of Drug + Ethyl cellulose

7.2.1.3 FTIR Analysis result of Drug + Eudragit RS **FTIR Analysis result of Drug + HPMC 6cps**

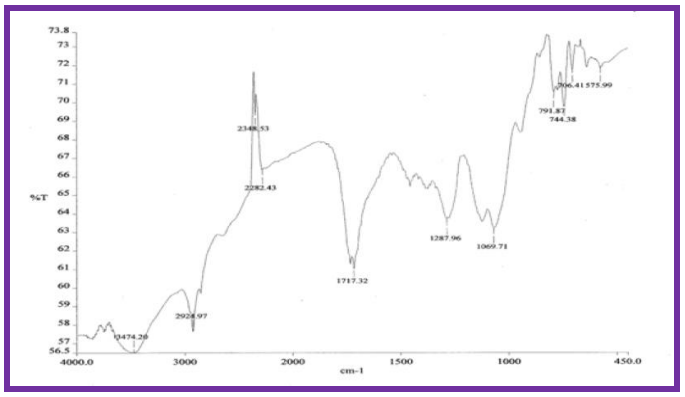


Fig.7.7 FTIR Analysis result of Drug + Eudragit RS

7.2.1.4 FTIR Analysis result of Drug + Eudragit L **Analysis result of Drug + HPMC 6cps**

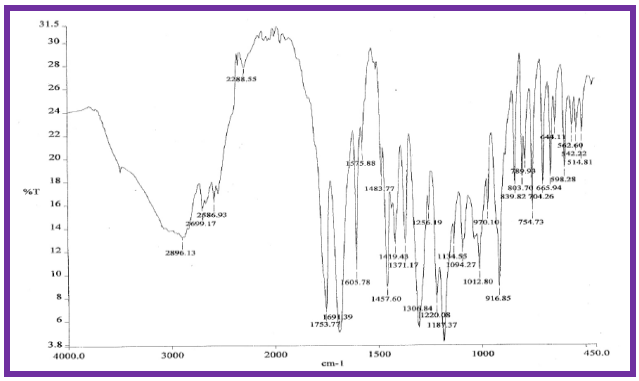


Fig.7.8 FTIR Analysis result of Drug + Eudragit L

CONCLUSION:

From the above FTIR Study and physical observation it was concluded that there was no significant Drug-Excipients interaction was observed. The results of FTIR study shown that there is no change in drug's melting peak after the preparation of tablet. So we

can conclude that drug and other excipients are compatible which each other.

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