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Development and evaluation of Bilayer Tablet of Metoclopramide HCl and Aceclofenac

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ABSTRACT

Bilayer tablets can be used to control the delivery rate of one or two different active pharmaceutical ingredients. Presently the use of bilayer tablets has been increased. Bilayer tablets can be a primary option to avoid chemical incompatibilities. The main goal of the present analysis work was to prepare bilayer tablet of Metoclopramide hydrochloride and Aceclofenac for separate layers to avoid the loss of dignity of the drug. Bilayer tablet manufacturing is addressed including material properties, lubrication, layer ordering, layer thickness, layer weight control, as well as first and final compression forces. These days, several pharmaceutical organizations are developing bilayer tablet for co-administration of drugs to improve the therapeutic efficacy as well as to reduce the chances of drug-drug interaction.

Keywords: *Bilayer tablet, Aceclofenac, Metoclopramide HCl.*

1. INTRODUCTION

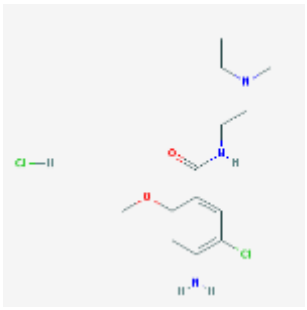
Description of Bi-layer tablet

A bilayer tablet is a double layer of closely packed atoms or molecules.

Bi-layer tablet is suitable for constant release of drugs in combination, And it separate two conflicting substances. One layer is immediate release like initial dose and Second Layer is service dose.

Metoclopramide Hydrochloride (IUPAC Name) 4-amino-5-chloro-N-[2-(diethylamino)ethyl]-2 methoxybenzamide monohydrochloride monohydrate

Chemical Formula: $C_{14}H_{23}Cl_2N_3O_2$



Metoclopramide Hydrochloride is one of the powerful anti-emetic drugs. Metoclopramide hydrochloride is a dopamine D2 antagonist that is used as an antiemetic. This agent may also increase the resting tone of the lower esophagus sphincter preventing acid reflux.

Therapeutic indication

- Prevention of delayed chemotherapy induced nausea and vomiting (CINV)
- Prevention of radiotherapy induced nausea and vomiting (RINV).
- Symptomatic treatment of nausea and vomiting, including acute migraine induced nausea and vomiting. Metoclopramide can be used in combination with oral analgesics to improve the absorption of analgesics in acute migraine.
- Prevention of delayed chemotherapy induced nausea and vomiting (CINV) as a second line option.

Mechanism of action

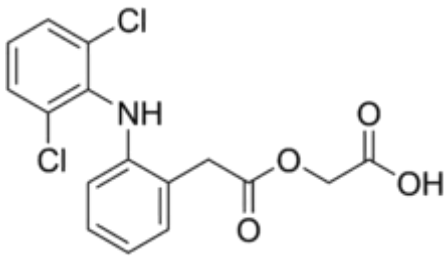
The antiemetic action of metoclopramide is due to its antagonist activity at D_2 receptors in the chemoreceptor trigger zone in the central nervous system — this action prevents nausea and vomiting triggered by most stimuli. At higher doses, 5-HT_3 antagonist activity may also contribute to the antiemetic effect.

The gastroprokinetic activity of metoclopramide is mediated by muscarinic activity, D_2 receptor antagonist activity, and 5-HT_4 receptor agonist activity. The gastroprokinetic effect itself may also contribute to the antiemetic effect. Metoclopramide also increases the tone of the lower esophageal sphincter.

Metoclopramide increases peristalsis of the duodenum and jejunum, increases tone and amplitude of gastric contractions, and relaxes the pyloric sphincter and duodenal bulb, while simultaneously increasing lower esophageal sphincter tone. These gastroprokinetic effects make metoclopramide useful in the treatment of gastric stasis (for example: after gastric surgery or diabetic gastroparesis), as an aid in gastrointestinal radiographic studies by accelerating transit through the gastrointestinal system in barium studies, and as an aid in difficult intubation of the small intestine.

Aceclofenac (**IUPAC Name)** 2-[2-[2-[(2,6-dichlorophenyl)amino]phenyl]acetyl]oxyacetic acid

Chemical Formula: $C_{16}H_{13}Cl_2NO_4$



Aceclofenac is a nonsteroidal anti-inflammatory drug It is used for the relief of pain and inflammation in rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. Aceclofenac is a crystalline powder with a molecular weight of 354.19. It is practically insoluble in water with good permeability. The drug works by inhibiting the action of cyclooxygenase (COX) that is involved in the production of prostaglandins (PG) which is accountable for pain, swelling, inflammation and fever.Some common adverse effects include gastro-intestinal disorders (dyspepsia, abdominal pain, nausea), rash, ruber, urticaria, symptoms of enuresis, headache, dizziness, and drowsiness .

Aceclofenac is a non-steroidal agent with marked anti-inflammatory and analgesic properties.The mode of action of aceclofenac is largely based on the inhibition to prostaglandin synthesis. Aceclofenac is a potent inhibitor of the enzyme cyclo-oxygenase, which is involved in the production of prostaglandins.

2. MATERIAL AND METHODS

Bilayer tablets containing Metoclopramide HCL and **Aceclofenac** were purchased from a local pharmacy in Bhopal, (M.P). Metoclopramide Hcl was obtained as a gift sample from SSUTMS Laboratory (Bhopal, India).

List of Materials:

- Aceclofenac
- micro crystalline cellulose MCC,
- PVP K-30
- Lactose.

Method

This is the techniques which are used to get the desired release profile. This process is used to determine excipient type, percentage, disintegration time.

Next step is the optimization it involves the use of 'mixture designs' for changing mixture composition and exploring how such changes will affect the properties of the mixture. The Main goal was to develop and optimize the fast disintegrating tablets Metoclopramide HCL with low friability and minimum disintegration time. And Talets prepared by wet granulation technique for oral delivery.

Processing Steps:

Step 1.) Collected Weighed quantity of the listed drugs. Which is listed above (List of Materials).

Step 2.) Then mixed uniformly with the help of mortar and pastel.

Step 3.) A solution prepared of alcohol and water in the ratio of 1:1.

Step 4.) To form a damp mass, Solution was added to drug excipient mixture.

Step 5.) Manually this damp was pass through the sieve no 18.

Step 6.) Then dried at 80°C for 5 to 6 hrs.

Step 7.) Then passed through 19 sieve.

Step 8.) 10% of the fines were added to the collected Granules.

Step 9). Now, added it with a solution of lubricant Magnesium stearate and colloidal silicon dioxide.

Step10.) Caution: Mixed it in a polyethylene bag for 5 to 6 minutes

Step 11.) At last, the granules were compressed using a multi-station tablet compression machine using 8 mm die containing 100mg.

Figure: Tablet compression machine

3. RESULTS AND DISCUSSION

For Aceclofenac:

Blend property of Aceclofenac:

The prepared granules were evaluated for the below blend properties.

- Bulk density
- Tapped density
- Carr's index
- Hausner ratio
- Angle of repose.

Bulk density	Obtained in Range of 0.233 to 0.381
Carr's index	Obtained 16.45%. i.e. in between of 10-20%.
Hausner ratio	1.4
Angle of repose.	< 35°

Results show that granules have satisfactory flow and required properties.

Evaluation of Aceclofenac conventional release tablet

Below Test conducted on compressed tablets:

- Thickness observed Uniform

- Hardness found ok.
- Tensile strength observed ok.
- Friability < 1% Observed.
- % drug content: Observed between 90-100%

Obtained Result satisfactory and within range.

For Metoclopramide HCL:

Blend Property

The prepared granules were evaluated for the below blend properties.

- Bulk density
- Tapped density
- Carr's index
- Hausner ratio
- Angle of repose.

Bulk density	Obtained in Range of 0.281 to 0.339
Carr's index	Obtained the range of 10-15% which was considered as excellent flow property.
Hausner ratio	1.5 indicates
Angle of repose.	Obtained less than 30° which gives good flow property to the granules.

Evaluation of Metoclopramide HCL

We evaluated the physical parameters of tablets and observed satisfactory.

Physical parameters of tablets are

- Thickness of the tablets
- Hardness of tablets
- Friability of tablets
- Disintegration time of tablets
- Wetting time of tablets
- Uniformity of weight of tablets.

After evaluation of tablets, result shows that all formulation have satisfactory properties.

4. CONCLUSION

Bilayer tablet showed good correlation of release profile and also fulfills all evaluation parameters with long time stability.

Bilayer tablet cannot degrade it will remain stable at different temp.

Bi-layer tablet of Metoclopramide HCL and Aceclofenac might be suitable for treatment of migraine by sequential release of the drug.

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