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Review Article

A Review on compatibility of "Sucralfate" in bi layer floating tablet for treatment of ulcer in pregnancy.

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ABSTRACT
To make a review by focusing upon characteristics of Sucralfate and its compatibility in Bilayer floating tablet for treatment of ulcer during pregnancy as Gastro Retaintive Drug Delivery System. This review focus on causes of stomach ulceration during pregnancy, characteristics study of Sucralfate and its compatibility with acceptance criterias of Bilayer Floating Tablet for treatment of ulceration during pregnancy .The ulcer protective Sucralfare is simpler and more effective H2 blockers. They can be implemented in case of pregnancy and administrated as combined form in empty stomach .Bi layer floating tablet is an approach of GRDDS. In Bi layered floating tablet ,Sucralfate can act as immediate release layer and absorbs at stomach and improve the bioavailability and which ideal dosage form attains the desired therapeutic concentration of drug in plasma and maintains constant frequency for entire duration of treatment.

Keywords: Sucralfate, Ulcerprotective, , Bilayered floating tablet,GRDDS.

INTRODUCTION

A stomach ulcer occurs when the mucus lining of the intestine or stomach erodes. The erosion affects acids of the stomach, and damages the stomach walls [1]*Antacids are commonly used for the treatment of Peptic Ulcer Diseases as they are considered safe during pregnancy .*

Sucralfate has no acid neutralizing action [2] *but delays gastric emptying—its own stay in stomach is prolonged. Sucralfate is minimally absorbed after oral administration. Its action is entirely local. It promotes healing of both duodenal and gastric ulcers. However, Sucralfate is frequently used now because its availability is simpler and more effective H2 blockers.*

Bi-Layered tablet contain immediate and sustained release layer.Theincorporated drug remain in gastric region[3] *for several hours and produce prolong gastric resistance time and improve bioavailability .It reduce drug waste and enhance the solubility of* [4]*drug. The drug release slowly at desired rate and increase GRT .and better control of fluctuations in plasma drug concentration*[5]
The present study focus on study about stomach ulceration during pregnancy, characteristics study of Sucralfate and the fulfilment of criteria of Bilayered Floating Tablet

Stomach ulcer during pregnancy

Causes of Stomach Ulcer during Pregnancy

An ulcer occurs due to an imbalance between digestive juices in the stomach and duodenum. Also, ulcers occur due to a bacterial infection called Helicobacter pylori (H. pylori).

Symptoms of Stomach Ulcer during Pregnancy

- *Nausea and vomiting*
- *Bloating*
- *Heartburn*
- *Severe pain in the middle or upper part of abdomen.*
- *Dark or black coloured stools due to bleeding.*
- *Weight loss*

Diagnosing Stomach Ulcer During Pregnancy

Esophagogastroduodenoscopy is the technique for the diagnosis of Stomach Ulcer Disease during pregnancy. However, the method is only used when the symptoms are severe. Also, when there are PUD-associated complications viz. Haemorrhages or Gastric outlet obstruction, this diagnosis works best.

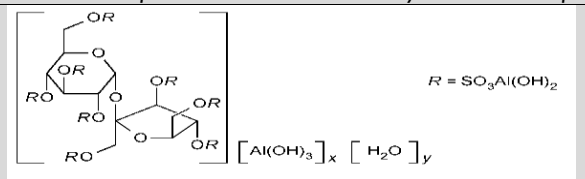
Table 1: Classification of drugs for the treatment of peptic ulcer

REDUCTION OF GASTRIC ACID SECRETION	H2antihistamines: *Cimetidine, Ranitidine, Famotidine, Roxatidine*	Proton pump inhibitors: *Omeprazole, Esomeprazole, Lansoprazole, Pantoprazole Rabiprazole Dexrabeprazole,*	Anticholinergic drugs: *Pirenzepine, Propantheline, Oxyphenonium*	Prostaglandin analogue: *Misoprostol*
NEUTRALIZATION OF GASTRIC ACID (ANTACIDS)	Systemic: *Sodium bicarbonate, Sod. citrate*	Nonsystemic: *Magnesium hydroxide, Mag. trisilicate, Aluminium hydroxide gel*		,
OTHERS	Ulcer protectives: *Sucralfate, Colloidal bismuth subcitrate (CBS)*	Anti-H. pylori drugs: *Amoxicillin, Clarithromycin, Metronidazole, Tinidazole, Tetracycline*		

MECHANISM OF ACTION OF SUCRALFATE

- *Ulcer protective Sucralfate [2] is a basic aluminium salt of sulfated sucrose*
- *Sucralfate polymerizes at pH < 4 by cross linking of molecules,*
- *It assume a sticky gel-like consistency.*
- *It strongly adheres to ulcer base, especially duodenal ulcer;*
- *remain there for ~ 6 hours.*
- *Surface proteins at ulcer base are precipitated, together with which it acts as a physical barrier preventing acid, pepsin and bile from coming in contact with the ulcer base.*
- *Dietary proteins get deposited on this coat, forming another layer.*

Table 2: Characteristics of sucralfate

Sl No	PARAMETERS	CHARACTERSTICS	Ref No
1	DESCRIPTION	*Sucralfate is white amorphous powder .Hydrous basic aluminium salt of sucrose octa sulphate. It is combination of Sucrose Sulphate and Aluminium hydroxide complex.*	*[7], [8]*
2	STRUCTURE		*[9]*
3	CHEMICAL NAME	Aluminiumhydroxide 1,3,4,6-tetra-O-sulfonato-β-D-fructofuranosyl,2,3,4,6-tetra-O-sulfonato-α-D-glucopyranoside	*[10]*
4	MOLECULAR FORMULA	*Al8(OH)16(C12H14O35S8)[Al(OH)3]x[H2O]y x=8 to 10, y=22 to 31*	*[11]*
5	MOLECULAR WEIGHT	*1577.823 g/mol*	*[12]*
6	SOLUBILITY	*Insoluable in water*	*[13]*
7	PHARMACOPOEIAL	*United State pharmacopoeia (USP) and*	*[14],*

	STATUS	*Indian Pharmacopoeia (IP)*	*[15]*
8	FDA APPROVAL	*US Food and Drug administration(USFDA) 10903*	*[16]*
9	NDA APPROVAL	*New drug Application(NDA) 018333*	*[17]*
10	ANDA APPROVAL	*Abbreviated New Drug Application(ANDA)074415*	*[18]*
11	PATENTS	*EPO 136100A2*	*[19]*
12	MECHANISM OF ACTION	*Sucralfate is H_2 receptor antagonist and basic aluminium saltof sulphated sucrose which polymerise at PH <4 by cross linking of molecules assuming gel like consistency and provide surface protein at ulcer base and act as physical barrier preventing acid pepsin and bile coming contact with ulcer base It has no acid neutralizing action but delay gastric emptying and remain in stomach for 6 hours*	*[20]*
13	PHARMACOKINETIC ACTION	*Absorb in GIT very small quantity(<2%), Distribute in inflamed GIT lesion, Metabolise no significant, Excreted in urine within 48 hrs.*	*[21]*
14	PHARMACODYNAMIC ACTION	*Relive the painful inflammation by creating a protective mechaninical barrier between lining of skin of GIT tract . Increase level of growth factors locally and increase in prostaglandin which is important in healing of mucosa (lining) of GIT.*	*[22]*
15	HALF LIFE	*1-2 hrs*	*[23]*
16	ROUTS AND TIME OF ADMINISTRATION	*Oral route as tablet or suspension in empty stomach.*	*[24]*
17	SITE OF ACTION	*Stomach*	*[25]*
18	DOSE	*Active Deodenal Ulcer – Adult dose-1g 4times per day, Maintenance dose- 1gm twice a day*	*[23]*
19	ADVERSE BDRUG REACTION	*It cause in place of GIT- constipation diarrhea,nausea, vomiting, gastric discomfort, indigestion,flatulence, dry mouth* Dermatological:*pruritus, rash,* Nervous System: *dizziness, insomnia, sleepiness, vertigo,* Other: *back pain,headache*	*[23]*
20	USES	*Treatmentof Peptic Ulcer Diseases(PUD) ,Gastroesophageal Reflx Disease (GERD), Heart burn(Pyrosis), Dyspesia (Indigestion) . Active duodenal ulcer.*	*[23]*
21	DRUG COMPATIBILITY	*Metoprolol Succinate*	*[26]*
22	OVERDOSE	*It occurs Dyspesia, Abdominal pain, Nausia Vomiting*	*[23]*
23	DRUG INTERACTION	*It interact with Digoxin, Ciprofloxacin ,Ofloxacin, Norfloxacin, Ketokinazole,Phenytoin, Quinidine, Tetracycline, Theophyline.*	*[27]*
24	STORAGE CONDITION	*Store it at room temperature (25°C).*	*[28]*
25	ACTION IN PREGNANCY AND LACTATION	*Sucralfate is acceptable to be used for pregnancy and lactation. It is categorised as AUTGApregnancycategory:B1 US FDA pregnancy category: B1 AU TGA pregnancy category B1: Drugs whichhave been taken by only a limited Number of pregnant women and women of child bearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed Studies in animals have not shown evidence increased occurrence of fetal damage. US FDApregnancy category B: It shows there are no adequate andwell-controlled studies in pregnant women.*	*[23]*

Table 3: Compatibility of Sucralfate with various criterias of bi-layered floating tablet

SL NO	CRITERIAS OF BILAYER FLOATING TABLET	PROPERTIES OF SUCRALFATE	REMARK
1	Drug should have less half-life (2-6 hrs).	1-2hrs	Compatible
2	Drug has less bioavailability in gastric region.	yes	Compatible
3	Unstable at intestinal pH	yes	Compatible
4	Long term treatment disease and drugs	Gastric Ulcer	Compatible
5	Less dose of drug	Max 1gm/day	Compatible
6	Less gastric retention time.	1hr maximum	Compatible
7	Narrow absorption window in GI tract	yes	Compatible
8	Basically absorbed from stomach and upper part of GIT.	yes	Compatible
9	Drugs that disturb normal colonic bacteria.	yes	Compatible
10	Locally active in stomach	yes	Compatible
11	Drugs that degrade in the colon		

Discussion

Sucralfate is USFDA A approved H_2 receptor antagonist and basic aluminium salt of sulphated sucrose which polymerise at PH <4 by cross linking of molecules assuming gel like consistency and provide surface protein at ulcer base and act as physical barrier preventing acid pepsin and bile coming contact with ulcer base It has no acid neutralizing action but delay gastric emptying and remain in stomach for 6 hours . Relive the painful inflammation by creating a protective mechanical barrier between lining of skin of GIT tract. Increase level of growth factors locally and increase in prostaglandin which is important in healing of mucosa (lining) of GIT. Treatment of Peptic Ulcer Diseases(PUD) Gastroesophageal Reflx Disease (GERD), Heart burn(Pyrosis), Dyspesia (Indigestion) . Active duodenal ulcer. Having half-life 1-2 hrs and dose Active Deodenal Ulcer – Adult dose-1g 4times per day, Maintenance dose- 1gm twice a day.

Conclusion

The above study conclude that the ulcer protective Sucralfare is simpler and more effective H2 blockers fulfilling all the criteria of Bilayer floating tablet .It can be implemented in case of pregnancy and lactation as a combined form in empty stomach As bi layered floating tablet Sucralfate can act as immediate release layer and improve the controlled delivery of drug for prolonged period of time at desired rate and improve the bioavailability and which ideal doses form attains the desired therapeutic concentration of drug in plasma and maintains constant frequency for entire duration of treatment. It can be implemented as a better formulation of GRDDS as future prospects.

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