For the last three centuries, Bismuth compounds have been of traditional importance for the treatment of infectious diseases, syphilis, amoebiasis, dyspepsia and diarrhea. Despite its old history, intensive research and investigation on the mechanism of action and its clinical efficacy has begun in recent years. Trivalent bismuth preparations such as bismuth subsalicylate (BSS) and colloidal bismuth subcitrate (CBS) are of most therapeutic efficacy amongst the available compounds. Indications for bismuth therapy in clinical practice are manifold. The fact that ulcer can develop with even normal acid secretion, prompted reexamination of ulcer therapy and renewed interest to try agents such as bismuth, that heal ulcers without reducing acid. Therapeutic efficacy of bismuth preparations are due to their cytoprotective and demulcent action. It coats the gastroduodenal mucosa especially ulcerated part and protects it against the digestive activity of acid and pepsin. It also increases prostaglandin synthesis which in turn increases mucous and bicarbonate secretion and reduces the H+ ion back diffusion.

Various studies have demonstrated the efficacy of bismuth compound in the healing of duodenal ulcer, 82% with CBS as compared to 43% with placebo at 4 weeks, three other studies compared CBS with ranitidine, showing 84% vs 78% healing rates respectively. Trials to see the efficacy of bismuth when combined with H2 receptor antagonists are very few, with inconclusive results. In gastric ulcer the results of bismuth therapy are similar to those of duodenal ulcer, being 72% as compared to 36% with placebo at 4 weeks and 96% with bismuth at 8 weeks. At present high relapse rates with various potent antiulcer drugs is the main problem to be solved especially after withdrawal of the treatment. Promising results have been reported for bismuth in duodenal as well as though less convincing in gastric ulcer. In a comparative study relapse rates at 4, 8 and 12 months were 41%, 55% and 62% respectively, as compared to 74%, 85% and 89% with ranitidine. Although these studies suggest superiority of bismuth in ulcer healing and reducing relapse rate, additional strategies are needed. Recent rediscovey of helicobacter pylori (HP) occupies a central place in the pathogenesis of ulcer disease. HP was found to be associated in upto 75% of gastric and over 90% of duodenal ulcer patients. Bismuth is active against HP and it also inhibits the proteolytic enzyme activity elaborated by this organism. In a comparative study of 3 weeks BSS, erythromycin and placebo showed clearance of HP in 78%, 7% and 0% respectively. Despite these encouraging results of short term bismuth therapy, relapse rate is still high. Long term eradication of FTP and concomitant gastritis was achieved when CBS was combined with amoxycillin or tinidazole. In a randomised trial of 8 weeks, eradication and healing was achieved in 27% cases receiving CBS plus placebo and 70% receiving CBS plus tinidazole, with a relapse rate of 68% and 44% respectively. The best results of over 90% are reported with triple regimen, i.e., combination of CBS for 4 weeks, tetracycline/amoxicillin and metronidazole for 2 weeks in duodenal ulcer patients, without any relapse for over 18 months. Unfortunately side effects noted with this regimen are unacceptable for some patients and it is yet to be decided which group of patients should be treated with this regimen. Bismuth compounds are also effective in the treatment of diarrhoea. The treatment of diarrhoea needs an anti-microbial agent to suppress the pathogen and an anti-secretory therapy to reduce fluid and electrolyte loss. BSS possesses both these properties, it has a direct anti-microbial activity against diarrhoeal pathogens, including toxigenic E. coli, Salmonella, Campylobacter jejuni ana clostridium difficile. It also binds enterotoxins excreted by toxigenic B. coli or
vibriocholera. Inspite of its antimicrobial activity there seems to be no change in overall composition of the gut flora. In the colon, BSS is converted to a variety of metabolic products which have less antimicrobial activity than the parent compound, but they suppress their metabolic activity like fermentation of lactose and raffirose, which in turn reduces flatulence and diarrhoea. In viral diarrhoea BSS inhibits plaque formation when given at high concentration. The salicylate component of BSS reduces the fluid loss in acute diarrhoea, perhaps by blocking prostaglandin synthesis and by inhibiting intestinal secretion by simultaneous Na+ and C reabsorption. Although BSS significantly reduces severity, duration of intestinal symptoms, stool weight and i/v fluid requirements in diarrhoea, it is too preliminary to make any definitive statement. Like other heavy metals bismuth has its own side effects and limitations of therapy. Clinically it results in apathy, mild a taxia and headache in the early phases to myoclonic jerks, dysarthria, severe confusion, hallucinations, epileptic seizures and even death in later phase. Extremely high levels of bismuth have been found in the brain, more so in grey matter with loss of purkinje cells in the cerebellum of such patients. However, it is generally accepted that the cessation of therapy may result in complete semission of symptoms with no sequelae. It has been shown that more than 99% of ingested bismuth is excreted in the faeces and a small quantity (0.2%) gets absorbed in the blood. Peak plasma levels are achieved after 30 minutes. Normal bismuth level in blood is ug/l and it may rise to over 50 ug/l with normal intake, but in patients with encephalopathy it may reach upto 2000 ug/l. Intestinal absorption of this heavy metal in multiple tissue sites is mainly responsible for its toxic effects which occur even with conventional doses given over a 6 weeks period and intestinal absorption may increase in patients with colitis. Urinary excretion is 2.6% per day. Most of the bismuth is excreted in the urine within 2-3 months, that is why it should not be given beyond 2 months with an abstinence period of at least 6-8 months. The salicylate component of bismuth compound is effectively absorbed and 95% of the oral dose can be recovered in the urine. With different dosage regimen, average peak plasma levels of salicylate were found considerably less than the toxic levels. However, caution should be exercised in prescribing to young children, individuals with salicylate sensitivity, bleeding disorders, renal disease and those taking drugs that have clinically significant interaction with salicylate.

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