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# DRUG-DRUG INTERACTIONS OF PANTOPRAZOLE: AN UPDATED REVIEW

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## ABSTRACT

Proton pump inhibitors (PPIs) are the most commonly used class of drugs in treating the gastric acid related disorders. Among them, pantoprazole is the most extensively prescribed drug in the clinical scenario. When compared to $H_2$ receptor antagonists, proton pump inhibitors had a high healing rate. In this review we mainly focused in reviewing the drug-drug interactions of pantoprazole. Among all the PPIs, the drug interaction profile of pantoprazole has been well established. When compared to omeprazole and esomaprazole, pantoprazole was associated with lower incidences of drug-drug interactions resulting either from their lower affinity for specific CYP isoenzymes or the involvement of additional elimination processes.

**KEYWORDS:** Drug-drug interactions, Pantoprazole, Proton pump inhibitors.

## INTRODUCTION

For treating the gastric acid related disorders, Proton pump inhibitors (PPIs) are the most commonly used class of drugs. Among them, pantoprazole is the most extensively prescribed drug in the clinical scenario. The food and drug administration (FDA) has approved the drug pantoprazole in the year 2000. When compared to $H_2$ receptor antagonists, proton pump inhibitors had a high healing rate in treating the gastric acid related disorders. Hence they are usually used in the treatment and management of peptic ulcer disease, gastroesophageal reflux disease and Zollinger-elison syndrome. They also play a major role in the eradication of H-pylori in peptic ulcer disease and can also be used as a prophylactic treatment for drug induced & stress induced peptic ulcers.[1-7]

## DRUG-DRUG INTERACTIONS

Usually these drugs can be used for prolonged time period which in turn increase the chance of causing drug-drug interactions with the concomitantly prescribed drugs.[8-10] Evidences were showing that pantoprazole had the low potential to cause drug- drug interactions when compared to omeprazole as it has high affinity for CYP 2C19 and moderate affinity for CYP 3A4. Co-administration of mycophenolic–mofetil with pantoprazole sodium results in decreased plasma concentration of mycophenolic acid in heart transplant recipients when compared to the administration of mycophenolic–mofetil alone. No significant changes in the pharmacokinetic parameters of heart or lung transplant recipients were observed when pantoprazole sodium was co-administered with the enteric coated mycophenolic sodium.[11,12]

A recent meta-analysis described the drug interactions between certain proton pump inhibitors and clopidogrel and these interactions were found to be mediated by CYP 2C19 which are of high clinical relevance.[1] Recent retrospective studies revealed that concomitant administration of clopidogrel with proton pump inhibitors reported some beneficial effects. But these beneficial effects are not observed in patients receiving pantoprazole sodium when compared to those patients who were under the treatment with omeprazole. Various studies revealed that being in steady state for omeprazole significantly decreased the exposure to the active metabolite and increased the total exposure to clopidogrel even after separating the administration of double doses of clopidogrel. After the substituting the omeprazole by pantoprazole sodium the differences become lowered significantly. This is consistent with the finding that clopidogrel must be activated by CYP2C19, an enzyme inhibited by omeprazole but not pantoprazole-sodium.[13-15]

According to a retrospective case control study, increased residual platelet aggregation and platelet activation was observed in the patients with coronary artery disease who were under the concomitant treatment with non-enteric coated acetyl salicyclic acid and proton pump inhibitors. A decrease in platelet aggregation was

observed with the co-administration of enteric coated acetyl salicyclic acid with pantoprazole sodium. No significant effect on the platelet activity in the levels of salicylates in the blood was observed with the administration of lansoprazole.[16-18]

Pantoprazole sodium has a low potential to interact with the other drugs was confirmed based on the extensive evidences available from both the healthy volunteer population and patient population. When combining pantoprazole sodium with the clopidogrel, diazepam, carbamazepine, clarithromycin, diclofenac, glibenclamide, ethanol, metoprolol, naproxen, levothyroxine, sustained release nifedipine, phenytoin, theophylline, tacrolimus, piroxicam, warfarin, cyclosporine, caffeine and antacids, there were no significant metabolic interactions were observed.[1,19] Pantoprazole sodium when combined with cisapride shows a minor interaction which is clinically insignificant.[20] At present pantoprazole magnesium was also available in the market where the drug interaction profiles were expected to be similar to that of the pantoprazole sodium.[1]

Pantoprazole may increase the effect or results in the toxicity with the co administration of amphetamines, raltegravir, saquinavir, topotecan, dexmethylphenidate, methotrexate, voriconazole, methylphenidate and fluconozole. When pantoprazole is co administered with the drugs like atazanavir, bisphosphonate derivatives, bosutinib, cefditoren, clopidogrel, dabigatran etexilate, dabrafenib, dasatinib, delavirdine, erlotinib, gefitinib, indinavir, iron salts, itraconazole, ketoconazole, mesalamine, multivitamins/minerals (with ADEK, folate, iron), mycophenolate, nelfinavir, nilotinib, posaconazole, rilpivirine, riociguat, risedronate and vismodegib the effects may be decreased.[21]

Among all the PPIs, the drug interaction profile of pantoprazole has been well established. When compared to omeprazole and esomaprazole, pantoprazole was associated with lower incidences of drug-drug interactions resulting either from their lower affinity for specific CYP isoenzymes or the involvement of additional elimination processes.

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