# Original article Utilization of Anti-peptic ulcer drugs in outpatient clinics of a tertiary hospital

# <sup>1</sup>Priti Pravin Dhande , <sup>2</sup>Hardik Rameshbhai Patel

<sup>1</sup>Associate Professor, Department of Pharmacology,Bharati Vidyapeeth Deemed University Medical College, Pune <sup>2</sup>3<sup>rd</sup> year MD Pharmacology Resident, Bharati Vidyapeeth Deemed University Medical College, Pune **Corresponding author:** Dr.Priti P. Dhande

#### Abstract

**Background:** Prescriptions of anti-peptic ulcer drugs are quite commonly found in outpatients as well as inpatients of all hospitals. The trend of using these drugs in unnecessary situations speaks about the overuse of such drugs.

Aim: To evaluate the percentage of various groups and drug combinations of anti-peptic ulcer drugs prescribed in outpatient clinics of a tertiary hospital.

**Methodology:** This was a cross-sectional observational study approved by the Institutional Ethics Committee. Data was collected from August-2013 to December-2013 by visiting different outpatient departments of the tertiary care hospital for two weeks each and reviewing the prescriptions during study period. Written informed consent was obtained from the prescribing doctors and patients for viewing their prescriptions.

**Results:** We found that out of 300 anti-peptic ulcer drugs prescribed, around 99% were prescribed by brand name. Amongst the APUDs, 31% drugs were in fixed dose formulations.

**Conclusion:** Proton pump inhibitors are the most common anti-peptic ulcer drugs prescribed. Fixed dose combinations and recently introduced drugs in this class of acid suppressants were very common in outpatient settings of the tertiary hospital. **Key words:** utilization, anti-peptic ulcer drugs, outpatients

#### Introduction

Anti Peptic Ulcer Drugs (APUDs) like proton pump inhibitors,  $H_2$ -receptor antagonists, antacids, synthetic prostaglandins, and cytoprotective agents are widely used nowadays and have changed the physicians' treatment patterns in general practice, gastroenterology as well as specialized clinics. The use of these drugs has been extended beyond prevention and treatment of peptic ulcers; to other disease and symptoms such as non-ulcer dyspepsia, heartburn, prevention of side effects caused by drugs, etc.<sup>1</sup>APUD overuse is common and this is evident across all specialties, particularly in those that commonly prescribe antiplatelet agents, nonsteroidal anti-inflammatory drugs (NSAIDs), steroids and anticoagulation medications. Recent concerns have arisen regarding the potential for adverse events involving long-term acid suppression." Inspite of being popularly prescribed worldwide, only few studies documenting their utilization could be found in Asian countries [China, Malaysia, Saudi Arabia, India]." Other studies found in literature have either focused on utilization of a single group of acid suppressants in patients or prescribing trends of these agents in specialty clinics like gastroenterology, critical care, orthopedic clinics, etc. Hence, this study was planned to evaluate the utilization of APUDs across all specialties in a tertiary care hospital of Western India.

# Methodology

This was a cross-sectional observational study approved by the Institutional Ethics Committee. Data was collected from August-2013 to December-2013 by visiting different outpatient departments of the tertiary care hospital for two weeks each and reviewing the prescriptions during study period. Written informed consent was obtained from the prescribing doctors and patients for viewing their prescriptions.

Approximately 1000 prescriptions were studied and 260 prescriptions containing anti peptic ulcer agents

found were analyzed in the study. Prescribed drugs were classified according to their pharmacological class. For information on cost, formulation, content, manufacturing company of the prescribed drugs-CIMS and Drug Today were referred. Prescribed drugs were categorized as single drugs or Fixed Dose Combinations (FDCs) and whether they were prescribed by generic or brand name. Collected data and all these details were entered in Microsoft Excel 2013. In this study, the percentage of cost difference in the maximum and minimum price of the same drug manufactured by different pharmaceutical companies has been calculated. The cost variation amongst the different anti-peptic ulcer drugs was calculated by the formula

 $\frac{[Cost of highest priced brand - Cost of lowest priced brand]}{Cost of lowest priced brand} \times 100$ 

### Results

Table.1– Demographic	characteristics of	patients p	prescribed a	nti-pep	tic ulcer	drugs

CHARACTERISTICS		PATIENTS n=260		
Age Gr	oup (years)			
•	0 - 20	24		
•	21-30	76		
•	31 - 40	42		
•	41-50	54		
•	51-60	35		
•	>60	29		
Gender	·			
•	Male	126		
•	Female	134		
Occupa	ation			
	Occupations requiring physical work	61		

<ul> <li>Office work</li> </ul>	47
<ul> <li>Non-working / Household work</li> </ul>	122
<ul> <li>Student</li> </ul>	30

Table 1 depicts that the most common age group in which APUDs were prescribed was 21-30 years. The prescriptions of these drugs did not differ among both the genders but there was a prominent population of patients who were non-workers or household workers in whom these were found to be prescribed more (46%).

Fig.1 - Distribution of anti-peptic ulcer drug prescriptions of the study in outpatients departments



Figure 1 shows that out of the 260 prescriptions of APUDs, around 73% prescriptions were found in orthopaedic [100(38%)] and medicine [91(35%)] departments. Anti-peptic ulcer drugs were least prescribed in Psychiatry, Ophthalmology and Paediatric OPDs.

Fig.2- Health problems in which anti-peptic ulcer agents were seen prescribed



Fig.2 shows the different health problems in which anti-peptic ulcer agents were prescribed as primary drug or coprescribed with other drugs. Highest number of such patients had musculoskeletal problems, followed by respiratory symptoms. Miscellaneous / other conditions included cases of plasmodium vivax malaria and viral fever, ophthalmic complaints, gynaecological problems (per-vaginal discharge), non-specific headache, vomiting, dizziness, weakness, sleep disturbances, weight gain, cold intolerance etc. Only 15 patients had complaints related to acid peptic disease in our study cohort.

CHARACTERISTICS	DRUGS (%) n=300	
Generic	4 (1.33)	
Branded	296 (98.67)	
Single drugs	205 (68.33)	
FDCs	95 (31.67)	
In patients with complaints / history of APD	71 (23.67)	
In patients without complaints / history of APD	229 (76.33)	
Drugs with complete instructions for use mentioned	5 (1.67)	
Drugs with no written instructions mentioned	295 (98.33)	
Duration of prescription		
<ul> <li>Duration not mentioned</li> </ul>	114 (38.0)	
<ul> <li>Once/Stat</li> </ul>	16 (5.33)	
• 3 Days	19 (6.33)	
• 5-7 Days	118 (39.33)	
• 10 days	16 (5.33)	
<ul> <li>14-15 Days</li> </ul>	15 (5.0)	
<ul> <li>30 Days</li> </ul>	2 (0.67)	

Table.2 – Characteristics of anti-peptic ulcer drugs prescribed

We found that out of 300 anti-peptic ulcer drugs prescribed, around 99% were prescribed by brand name. Amongst the APUDs, 31% drugs were in fixed dose formulations. [Table 2]Nearly 76% of these drugs were given in patients who had no presenting acid-peptic symptoms. It was also observed that only 2% anti-peptic ulcer drugs were prescribed with complete written instructions for their use. Other surprising fact found was that 38% drugs were prescribed with no mention of their duration of use in prescriptions. Among rest of the prescriptions where duration of use was mentioned, majority of them were prescribed for one week. More than two APUD drugs were found in 24 Prescriptions. In 15 such patients proton pump inhibitors were given with antacids, in 5 patients proton pump inhibitors were given with sucralfate and in 4 patients  $H_2$  blocker was given with antacids.





As seen in figure 3, majority (86%) of anti-peptic ulcer drug formulations prescribed were oral solid formulations – tablets or capsules. Liquid preparations constituted 8% of the total formulations which mainly comprised of antacid combinations. Injectable formulation was prescribed quite less (5%) as compared to the above dosage forms which

included intravenous pantoprazole (12 prescriptions) and ranitidine (4 prescriptions). A small percentage (1%) of patients was prescribed a newer formulation of proton pump inhibitor which is available in the form of rapidly acting (insta) granules.

Fig.4 Anti-peptic ulcer drugs prescribed in the study



Fig.4 shows the variety and proportion of anti-peptic ulcer drugs found in the study prescriptions. Most common class of anti-peptic drug ulcer prescribed was Proton Pump Inhibitors (71%) followed by  $H_2$ blockers (19%) and Antacids (7%). We also found 7 prescriptions (3%) with Sucralfate as the gastroprotective. Of all these drugs, Pantoprazole was prescribed the most (27%) followed by Dexrabeprazole (23%). Less prescribed PPIs (1%)were Ilaprazole and Lansoprazole. Ranitidine was the only H<sub>2</sub> blocker that was found in the prescriptions.

ANTI-PEPTIC ULCER DRUGS	NUMBER OF FDCs (%) n=95
Proton Pump Inhibitors + Prokinetic Agents	65 (68.42)
Antacid Combinations	19 (20.00)
Sucralfate + Oxethazaine	6 (6.32)
Proton Pump Inhibitors + NSAIDs	2 (2.10)
Proton Pump Inhibitors + Buffer	2 (2.10)
H <sub>2</sub> blockers + Prokinetic Agents	1 (1.05)

**Table.3** Fixed dose combinations of anti-peptic ulcer drugs prescribed

Most common FDC (Table 3) was Proton Pump Inhibitor + Prokinetic Drug (68%) and frequently prescribed such FDC was Pantoprazole + Domperidone (36.84%). Domperidone and Levosulpiride were the prokinetic agents found in combination with these prescribed drugs. The only Proton Pump Inhibitor + NSAID combination seen in these prescriptions was Rabeprazole + Diclofenac.

Table.4 – Average price of different formulations of APUD prescribed

Formulations	Price INR (Mean ± SD)
Capsule/Tab	$6.02 \pm 3.98$
Injection	41.6 ±22.42
Liquids (Syrup/Gel/Solution)	58.37 ± 28.52
Granules	$9.25 \pm 0.00$

The cost of different formulations of APUDs seen prescribed in this study was calculated. Table 4 depicts the average price (rupees) of the formulations found in the study prescriptions for single dose except liqu-ids. As the liquid preparations of these drugs are available in varying quantities, we have only calculated the average cost of these formulations per bottle of drug.

**Table.5-** Percentage cost variation among various APUDs prescribed in the study

Drug	Min market	Max market	Avg price in	% cost
(strength in mg of tablet/capsule)	price Rs.	price Rs.	study Rs.	variation
Dexrabeprazole (10)	3.5	12	6.9	242.85
Dexrabeprazole + Domperidone (10+30)	3.99	11.45	7.9	186.96
Esomeprazole (20)	1.7	5.7	3.2	235.29
Esomeprazole (40)	2.7	9.09	5.4	236.66
Esomeprazole + Domperidone (40+30)	3	11.5	8.75	283.33
Ilaprazole (10)	6.9	8.04	8.04	15.94

Pantoprazole (40)	2.55	7.6	5.46	198.03
Pantoprazole 40mg Injection-vial	44	85	54.21	93.18
Pantoprazole + Domperidone (40+30)	3.9	11.7	9.69	200
Ranitidine (150)	0.42	1.9	0.546	352.38
Ranitidine 50mg/2ml Injection-ampule	2.34	15.25	3.47	551.7
Ranitidine + Domperidone (150+10)	0.22	2.45	0.548	1013.63
Rabeprazole (20)	1.03	8	2.57	676.69
Rabeprazole + Domperidone (20+30)	3.9	9.9	6.19	153.84
Rabeprazole + Diclofenac (20+100)	3.4	5.6	5.6	64.7
Omeprazole (20)	1.9	10.48	5.44	451.57
Omeprazole + Domperidone (20+10)	1.4	8.3	7.06	492.85

Above table 5 summarizes the most frequently prescribed PPIs,  $H_2$  blocker and their FDCs with minimum and maximum cost of their formulations available in the Indian market. Percentage cost variation has been calculated for these drugs and Tablet Ranitidine 150mg + Domperidone 10mg shows maximum cost variation (1013.63%) followed by Rabeprazole 20 mg (676.69%). The least cost variation is seen with the newer PPI named Ilaprazole 10 mg tablets (15.94%).

## Discussion

This study is the first one of its kind in which all the groups of anti-peptic ulcer drugs have been reviewed in multiple specialities of a hospital. Literature search has shown that studies have either concentrated on one particular acid suppressant group like PPI<sup>,</sup> or authors have done such studies in speciality clinics gastroenterology, Intensive like care units, hospilitalized patients,' orthopaedic clinics or on discharge letters to study their utilization. The results of this study show that three out of four APUDs prescribed were either from orthopaedic or medicine OPDs (Fig.1). Doctors from the department of psychiatry were seen quite cautious about using APUDs- only one prescription of APUD was found

in two weeks duration. This observation was justified, as the psychiatrists routinely prescribed drugs which were least gastro-irritant and they only preferred to prescribe APUDs in patients with significant history of acid peptic symptoms. Similarly, less utilization of these APUD drugs was also seen in ophthalmology and paediatric department which is rationally jus-tified. Different formulations of APUDs prescribed on OPD basis were also studied (Fig.3).In the present study, 95% APUDs were prescribed by oral route and the commonest form was tablets (67%) followed by caps-ules (19%) and liquid formulations (8%). Use of injectable preparations of APUDs was 5% in the current study which was similar with the average results (6.85 %) of drug utilizations studies on different classes of drugs in various parts of India. "" In the present study, 2 prescriptions had OmezInsta (Omep-razole 20mg + Sodium bicarbonate 1680 mg buffer) granules as a newer formulation of PPI in them (Fig-.3). It is an advanced formulation of Omeprazole, internationally referred to as IR-Ome (Immediate Rel-ease Omeprazole).In this study (Fig.4), most commonly prescribed class of APUDs was found to be PPIs (71%) followed by H<sub>2</sub> Blockers

(19%), Antacids (7%) and then Sucralfate (3%). Many studies have shown contrasting results in which  $H_2$  blockers were predominantly prescribed as compared to PPIs.**Error! Bookmark not defined. Error! Bookmark not defined. Error!** 

**Bookmark not defined.** We also came across some recent APUD utilization studies which support the present study results wherein it was found that PPIs were the most common class of APUDs prescribed.<sup>...</sup>

In the PPI class of drugs, Pantoprazole (27%) and Dexrabeprazole (23%) were the commonest individual APUDs prescribed (Fig.4). Drug utilisation studies showing commonly utilised PPI:

Author	Published Year	Country	Most Common PPI
Niklasson et al	2003	Swedan	Lansoprazole
Ajay et alError! Bookmark	2003	India	Pantoprazole
not defined.			
Heidelbaugh J et al	2006	USA	Pantoprazole
Dirk Ahrens et al Error!	2010	Germany	Pantoprazole
Bookmark not defined.			
Vipin et al	2011	India	Omeprazole
Katherine et alError!	2011	USA	Esomeprazole
Bookmark not defined.			
Marwan et al <b>Error!</b>	2012	Labenan	Rabeprazole
Bookmark not defined.			

In a study conducted in the orthopedics outpatient department of an urban, tertiary care, medical college hospital in West Bengal (2012), an exactly different situation was seen. Here H<sub>2</sub> blockers were the most commonly used gastroprotective agents and Famotidine was the predominantly prescribed drug from this class. Error! Bookmark not defined. FDCs should always be based on convincing therapeutic justification. Each fixed dose combinati-on should be carefully justified and clinically relevant to whom it is prescribed. In the present study most commonly (68.42%) found FDCs of APUDs were PPI with prokinetic agents (Table.3). Ren et al in 2014 in a meta-analysis showed that addition of prokinetics with PPI in gastroesophageal reflux disease may only partially improve patient quality of life, but has no significant effect on symptom or endoscopic response of GERD. Different antacid combinations prescribed in the study contained magnesium and alluminium salts with oxethazaine, simethicone, carboxymethyl cellulose and activated charcoal.

Indian markets are flooded with a huge number of branded formulations, available for every drug molecule, with simultaneous pricing difference between the different brands of the same formulation. The rising price of drugs in India would soon make it difficult for medicines to reach a broad fraction of the population. This may be due to complex socioeconomic reasons, including a number of factors e.g. not following the Essential Drug List, an imperfect drug distribution system, irrational use of medicines, misuse of drugs, multiple prescribing to name a few. Due consideration must be placed on pricing of drugs in the EDL, to increase their accessibility to common people. Drug Price Control Order (DPCO) appears to be an effective tool to keep in rein the drug prices. A study in the United States found drug prices to be high and that price discrimination occurred across the industry. But very less studies are available in our scenarios which compare the cost of drugs of different brands.' Therefore we decided to compare the cost of different brands of anti-peptic ulcer drugs as they are very frequently found in prescriptions. (Table 5) The drug prices available in CIMS & Drug Today w-ere compared, as they are commonly referred source of drug information and are updated regularly. It is observed from our results that there is a wide (up to 1013.63%) variation in prices of these drugs manufactured by different pharmaceutical companies. The least cost variation is seen with the newer PPI named Ilaprazole (15.94%). This might be due to the fact that the drug is not yet manufactured by many pharmaceutical companies and hence available options do not vary much in their prices. A study on percentage cost variation of antidiabetic drugs done by Jadhav NB et alError! Bookmark not defined. concludes that as the number of manufact-uring companies increases, the percent price variation also increases. The reasons for this price variation could be as

follows:- Error! Bookmark not defined."

- The existing market structure of the pharmaceutical industry
- Asymmetry of information or imperfect information
- Industry costs and government regulations and pricing policies
- Costs of raw supplies, distribution and promotion
- Economic goals of the parent company, target return on investment

It is felt that physicians could provide better services and reduce costs of drugs if information about drug prices was readily available. Studies have shown that providing a manual of comparative drug prices annotated with prescribing advice to physicians reduced their patients' drug expense. A study by Philip S et al has concluded that percentage price variation between different fast moving brands in the therapeutic classes of Analgesics, Antiasthma, Antibiotics, Cardiovascular, Antidiabetics, Antiulcer, Hypolipidemics and Antipsychotics varies from 33%-1620%. A price corridor should be fixed for brands coming under these generics to prevent exploitation of patients.

## Conclusion

Proton pump inhibitors are the most common antipeptic ulcer drugs prescribed. Fixed dose combinations and recently introduced drugs in this class of acid suppressants were very common in outpatient settings of the tertiary hospital.

#### References

 Kenneth R. McQuaid. Drugs Used in the Treatment of Gastrointestinal Diseases. In: Bertram GK atzung, Susan B Masters, Anthony J Trevor. Basic & Clinical Pharmacology.12<sup>th</sup>Edition.New Y-ork: Mcgraw Hill; 2012:1081-1114

- Chong VH, Tengah DS, Zolkipli MK. Acid suppression therapy: overused and difficult to cont-rol. South Med Journal. 2010 Jul;103(7):713-4
- 3. Cote G, Howden C. Potential adverse effects of proton pump inhibitors. Current gastroenterology reports. 2008 June;10(3):208-214.
- 4. Inadomi J, Fendrick A. PPI use in the OTC era: Who to treat, with what, and for how long?. Clin-ical Gastroenterology and Hepatology. 2005;3(3):208-215.
- 5. Jacobson BC, Ferris TG, Shea TL, Mahlis EM, Lee TH, Wang TC. Who is using chronic acid su-ppression therapy and why?. Am J Gastroenterol. 2003 Jan;98(1):51-8
- 6. Zeng W, Finlayson AE, Shankar S, Bruyn W and Godman B. Prescribing efficiency of proton pu-mp inhibitors in China: influence and future directions. BMC Health Services Research (2015) 1-5:11
- Almeman A, Alkhoshaiban AS and Rasool S. Prescribing Practices and Cost of Drugs for Peptic Ulcer in a Primary Health Center in Pulau Penang, Malaysia. Tropical Journal of Pharmaceutical Research August 2013; 12 (4): 629-634
- Alsultan MS, Mayet AY, Malhani AA, Alshaikh MK. Pattern of Intravenous Proton Pump Inhibi-tors Use in ICU and Non-ICU Setting: A Prospective Observational Study. The Saudi Journal of Gastroenterology 2010 16(4):275-9
- 9. John LJ, Devi PD, Shoba G. Utilization Profile of Gastrointestinal Medications among the Critic-ally Ill Patients of A Tertiary Care Hospital. Jordan Journal of Pharmaceutical Sciences, Volume 6, No. 3, 2013
- Shankar P, SubishP B, Mishra P, Saha A. Ambiguous pricing of topical dermatological products: A survey of brands from two South Asian countries. Journal of Pakistan Association of Dermato-logists. 2006;16:134-40
- 11. Pang S, Graham D. Review: A clinical guide to using intravenous proton-pump inhibitors in refl-ux and peptic ulcers. Therapeutic advances in gastroenterology. 2010;3(1):11-22
- 12. Tsoi K, Hirai H, Sung J. Meta-analysis: comparison of oral vs. intravenous proton pump inhibi-tors in patients with peptic ulcer bleeding. Alimentary pharmacology & therapeutics. 2013;38(-7):721-728
- Mostaghni AA, Hashemi SA, Heydari ST. Oral omeprazole and IV pantoprazole had equal effect-ts on prevention of rebleeding after endoscopic therapy in patients with high risk bleeding peptic ulcers. Iran Red Crescent Med J 2011; 13(7):458-463
- 14. Kaur S, Rajagopalan S, Kaur N, Shafiq N, Bhalla A, Pandhi P et al. Drug Utilization Study in M-edical Emergency Unit of a Tertiary Care Hospital in North India. Emergency Medicine Internat-ional. 2014;2014
- 15. Erdeljic V et al. Use of gastroprotective agents in recommended doses in hospitalized patients receiving NSAIDs: a drug utilization study.Pharm World Sci. 2006 Oct;28(5):318-25
- 16. Nardino R, Vender R, Herbert P. Overuse of acid-suppressive therapy in hospitalized patients. The American journal of gastroenterology. 2000;95(11):3118-3122
- Kumar A, Dalai C, Ghosh A, Ray M. Drug utilization study of co-administration of nonsteroidal antiinflammatory drugs and gastroprotective agents in an orthopaedics outpatients department of a tertiary care hospital in West Bengal. International Journal of Basic & Clinical Pharmacology. 2013;2(2):199-202

- Ahrens D, Chenot J, Behrens G, Grimmsmann T, Kochen M. Appropriateness of treatment recommendations for PPI in hospital discharge letters. European journal of clinical pharmacology. 20-10;66(12):1265-71
- 19. Thakkar K, Suman S, Billa G, Thakkar M. A Drug Utilization Study of Cognition Enhancers in Dementia in a Tertiary Care Hospital in Mumbai. J ClinDiagn Res. 2014 May;8(5):HC05-8
- 20. Taskeen M, Anitha N, Ali S, Bharath R, Khan A. A study on rational drug prescribing pattern in geriatric patients in hyderabad metropolitan. Journal of Drug Delivery & Therapeutics. 2012;2(5): 109-113
- 21. Jadhav P, Moghe V, Deshmukh Y. Drug utilization study in ophthalmology outpatients at a terti-ary care teaching hospital. ISRN pharmacology. 2013;2013
- 22. Thiruthopu N, Mateti U, Bairi R, Sivva D, Martha S. Drug utilization pattern in South Indian pe-diatric population: A prospective study. Perspectives in clinical research. 2014;5(4):178-83
- 23. Thakkar K, Jain M, Billa G, Joshi A, Khobragade A. A drug utilization study of psychotropic dr-ugs prescribed in the psychiatry outpatient department of a tertiary care hospital. Journal of clini-cal and diagnostic research: JCDR. 2013;7(12):2759-64
- 24. Adhikari A, Biswas S, Gupta R. Drug utilization pattern in pregnant women in rural areas, India: Cross-sectional observational study. Journal of Obstetrics and Gynaecology Research. 2011;37(-12):1813-1817
- Dr. Reddy's launches 'OmezInsta' Immediate Release Omeprazole in sachets. Available at (La-st Accessed on 29/10/2015) http://www.drreddys.com/media/popups/may22\_2008.htm
- Heidelbaugh J, Inadomi J. Magnitude and economic impact of inappropriate use of stress ulcer prophylaxis in non-ICU hospitalized patients. The American journal of gastroenterology. 2006;10-1(10):2200-05
- 27. Sheikh-Taha M, Alaeddine S, Nassif J. Use of acid suppressive therapy in hospitalized non-criti-cally ill patients. World journal of gastrointestinal pharmacology and therapeutics. 2012;3(6):93-96
- 28. Carey K, Cross J, Silva M, Stefan M, Rothberg M. Pharmacy student impact on inappropriate pr-escribing of acid suppressive therapy. American journal of pharmaceutical education. 2011;75(-9):175
- 29. Pham C, Regal R, Bostwick T, Knauf K. Acid suppressive therapy use on an inpatient internal m-edicine service. Annals of Pharmacotherapy. 2006;40(7-8):1261-1266.
- Niklasson A, Bajor A, Bergendal L, Simren M, Strid H, Bjornsson E. Overuse of acid suppressive therapy in hospitalised patients with pulmonary diseases. Respiratory medicine. 2003;97(10):114-3-50
- Heidelbaugh J, Inadomi J. Magnitude and economic impact of inappropriate use of stress ulcer prophylaxis in non-ICU hospitalized patients. The American journal of gastroenterology. 2006;10-1(10):2200-05
- Vipinkumarsingh et al. Prescribing pattern of acid suppressants in modern clinical practice An analysis. Der Pharmacia Sinica. 2011; 2(3):67-73
- Ren L, Chen W, Qian L, Li S, Gu M, Shi R. Addition of prokinetics to PPI therapy in gastroesop-hageal reflux disease: A meta-analysis. World journal of gastroenterology: WJG. 2014;20(9):241-2-19

- 34. Das S C, Mandal M, Mandal S C. A critical study on availability and price variation between dif-ferent brands: Impact on access to medicines. Indian Journal of Pharmaceutical Science. 2007;69-(1):160-63
- Monaghan M, Monaghan M. Do market components account for higher US prescription prices?. Annals of Pharmacotherapy. 1996;30(12):1489-94
- Jadhav N, Bhosale M, Adhav C. Cost analysis study of oral antidiabetic drugs available in Indian market. IJMRHS. 2013; 2(1): 63-69
- 37. Karve A, Chattar K. Cost analysis study of oral antihypertensive agents available in Indian mark-et. International Journal of Basic & Clinical Pharmacology. 2014;3(3):479-83
- 38. Sarkar P. A rational drug policy. Indian J Med Ethics. 2004;1:11-2
- 39. Rataboli P, Dang A, others. Antimicrobial price variation: Conundrum of medical profession!. Journal of postgraduate medicine. 2007;53(1):72-74
- 40. Frazier L, Brown J, Divine G, Fleming G, Philips N, Siegal W et al. Can physician education lo-wer the cost of prescription drugs? A prospective, controlled trial. Annals of internal medicine. 1991;115(2):116-21
- 41. Philip S and Revikumar KG. A Study on the Prices of some Branded Drugs of eight Therapeutic Categories. Hygeia.J.D.Med. 2012; 4 (2): 78-86