

Research Article

Economic analysis of oral cephalosporins in the Indian market

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ABSTRACT

Background: Bacterial infections require appropriate and affordable treatment. A number of antimicrobial formulations are available in the Indian scenario. Affordable prescriptions improve compliance rate of the patients. This study was planned to evaluate & analyse the variation in the cost of oral cephalosporins (single and combination) in the Indian market.

Methods: Cost per tablet or capsule of cephalosporins being manufactured by different companies, in the same strength and dosage forms was obtained from two drug compendia. The difference in the maximum and minimum price and percentage variation in price was calculated.

Results: There are a number of companies manufacturing a particular drug, eg. Tab Cefixime (200 mg) - 127 companies, Tab Cefpodoxime (200 mg) - 106 companies, Cap Cefalexin (500 mg) - 38 companies and amongst the combinations; Tab Cefixime (200 mg) + Tab Clavulanate (125 mg) - 51 companies, Tab Cefpodoxime (200 mg) + Tab Clavulanate (125 mg) - 32 companies. A wide variation was found amongst the drugs ranging from 1746% for Tab Cefpodoxime (200 mg) to just 8.4% for Tab Cefdinir (100 mg). A similar variation existed for the combination drugs 9900% for Tab Cefixime (250 mg) + Tab Ornidazole (500 mg) and 42.1% for Tab Cefpodoxime (200 mg) + Tab Ofloxacin (200 mg).

Conclusions: This study shows a wide price variation of the same drugs manufactured by different companies. The manufacturing companies must aim to reduce the price variation while maintaining the quality and therapeutic efficacy in order to benefit patients and practitioners.

Keywords: Pharmacoeconomics, Cephalosporins, Pricing strategy, DPCO 2013, Indian patent act 2005, WHO guide to good prescribing, Reasons for price variation

INTRODUCTION

Bacterial infection such as lower respiratory tract infections (LRTI) is a leading cause of death in low-income and the 3rd leading cause of death in middle-low income countries.¹ They account for about 91 deaths and 53 deaths per 1 lac population in the two groups respectively.¹ Thus, there exists a high burden of bacterial disease and the presence of risk factors for its emergence and spread in the developing countries.

Availability of life-saving antimicrobials is of paramount importance in all countries afflicted by such infectious

diseases. There exists a wide range of obstacles to the adequate access to these drugs. Issues of financing, pricing, supply, selection and distribution are crucial in this respect.

Pricing of drugs is a major factor influencing the health expenditure of the world's poor. Unaffordable treatments in developing countries are a source of welfare losses and hampers growth by making the health capital obsolete. In developing countries 50 to 90 percent of drugs are paid out-of-pocket as a share of total health expenditures.² Appropriate and good quality drugs are imperative for the benefit of patients and also at an affordable price.

With the growth of Indian pharmaceutical industry, Indian market is flooded with branded generic drugs with a lot of variation in the cost of different brands of the same formulation.³ This exuberant pricing is a major concern to both physician and patient. It also forms an important determinant factor influencing the compliance to treatment.

Cephalosporins, β lactam antibiotics, are primarily indicated for the prophylaxis and treatment of bacterial infections caused by both gram positive as well as gram negative organisms.⁴⁻⁶ Successive generations have a broad spectrum of activity, especially against hospital acquired infections, infections caused by *Klebshiella*, *Enterobacter*, *Proteus*, also against sexually transmitted diseases (STDs), meningitis, community acquired pneumonia, to name a few.⁴⁻⁶ In the Indian market, oral cephalosporins are available in various brands. Prices of these medicines vary a lot and prescribing a cheaper brand will be an economically viable option to the patient.

In this context, this price variation of oral cephalosporins needs to be monitored. Furthermore, to the best of our knowledge no study is available which compares the cost of oral cephalosporins of different brands. So, we decided to carry out the study with the objective to project a representative view of the existing situation, by collecting data about the cost of common oral cephalosporin drugs available either singly or in combination, number of manufacturing companies for each and, to evaluate the difference in cost of different brands of same active drug by calculating percentage variation of cost.

METHODS

The study was conducted in the Department of Pharmacology at a tertiary care hospital December 2014. Price of the drugs per tablet or capsule were reviewed from “Current Index of Medical Specialties” July-October 2014 and “Indian Drug Review” Vol. XXI, Issue No.4, 2014 for analysis of different formulations of oral cephalosporins.

The retail cost of a particular drug being manufactured by different companies, in the same strength, number and dosage forms was compared. The drug formulation being manufactured by only one company was excluded can be deleted. Difference between the maximum and minimum prices of the same drug manufactured by different pharmaceutical companies was calculated. Percentage price variation was calculated by:

$$\% \text{ Price variation} = \frac{\text{Maximum price} - \text{Minimum price}}{\text{Minimum price}} \times 100$$

RESULTS

Prices of 8 oral cephalosporins were availed from the compendia. Similarly 8 cephalosporins in combination with different drugs were derived. These 16 products exist in 42 different formulations manufactured by different pharmaceutical companies. Individual prices of these formulations were analysed. There exists an extreme wide variation in the percentage price of the drugs which was found to be above 100% in most of the cases and a few of them even went above 1000%.

Table 1: Price variation between 1st generation cephalosporins.

Drugs	Formulations	Doses (mg)	Manufacturing companies	Min Price per tablet (INR)	Max Price per tablet (INR)	% Price Variation
Cefadroxil	4	Tab 125	27	0.9	2.5	177
		Tab 250	32	1.9	6.0	215
		Tab 500	28	3.3	8.5	157
		Cap 500	5	3.6	10.6	194
Cefalexin	4	Tab 125	19	1.9	4.9	157
		Tab 250	26	3.0	10.1	236
		Cap 500	38	6.3	50	693
		Tab 750	8	18.0	23.9	32.7

Single drug therapy

There are a number of companies manufacturing a particular drug, eg. Tab Cefixime (200mg) - 127 companies, Tab Cefpodoxime (200mg) - 106 companies, Cap Cefalexin (500mg) - 38 companies. Table I shows the price variation between 1st generation cephalosporins. In this group, Cefalexin (Cap 500mg) shows maximum

price variation of 693%, while Cefalexin (Tab 750mg) shows minimum variation of 32.7%.

Table II shows the price variation between 2nd generation cephalosporins. In this group, Cefuroxime (Tab 500 mg) shows maximum price variation of 1696%, while Cefaclor (Tab 250 mg) shows minimum variation of 55%. Table III shows the price variation between 3rd

generation cephalosporins. In this group, Cefpodoxime (Tab 200mg) shows maximum price variation of 1746%, while Cefdinir (Tab 100mg) shows minimum variation of 8.4%.

Combination therapy

In Combination therapy, total 8 combinations were analysed (6-3rd generation and 2-2nd generation combinations). In this, numbers of companies manufacturing a particular drug combination were Tab

Cefixime (200mg) + Tab Clavulanate (125mg) - 51 companies, Tab Cefpodoxime (200mg) + Tab Clavulanate (125mg) - 32 companies.

Cefuroxime (250mg) and Clavulanate (125mg) combination shows the maximum variation (320 %) amongst the 2nd generation drugs while Cefixime (200mg) and Ornidazole (200mg) combination shows the maximum variation (9900 %) amongst the 3rd generation drugs. Table IV shows price variation in combination drug therapy

Table 2: Price variation between 2nd generation cephalosporins.

Drugs	Formulations	Doses (mg)	Manufacturing companies	Min Price per tablet (INR)	Max Price per tablet (INR)	% Price Variation
Cefaclor	2	Tab 250	4	18.7	29.0	55
		Tab 375	4	34.5	93.8	171
Cefuroxime	3	Tab 125	20	6.25	19.95	219
		Tab 250	88	7.8	43.75	460
		Tab 500	96	4.8	86.25	1696

Table 3: Price variation between 3rd generation cephalosporins.

Drugs	Formulations	Doses (mg)	Manufacturing companies	Min Price per tablet (INR)	Max Price per tablet (INR)	% Price Variation
Cefdinir	4	Tab 100	2	8.3	9.0	8.4
		Tab 125	2	1.0	1.2	20
		Cap 300	11	21.0	62.5	197
		Tab 500	2	25.0	78.0	212
Ceftamet	2	Tab 250	5	13.1	25.2	92.3
		Tab 500	5	26.3	45.6	73.3
Cefixime	5	Tab 100	106	3.7	18.9	410
		Cap 100	2	3.0	3.4	13.3
		Tab 200	127	27.0	49.0	81
		Cap 200	2	50.0	58.25	16.5
		Tab 400	7	15.8	30.0	89.87
Cefpodoxime	2	Tab 100	100	5.4	26.8	396
		Tab 200	106	1.95	36.0	1746

Table 4: Price variation in combination drug therapy.

Drugs	Formulations	Doses (mg)	Manufacturing companies	Min Price per tablet (INR)	Max Price per tablet (INR)	% Price Variation
Cefuroxime + Clavulanate (125 mg)	2	250	6	16.5	69.3	320
		500	4	30.2	48.0	58.94
Cefixime + Azithromycin (250 mg)	1	200	10	16.0	31.0	93.75
Cefixime + Clavulanate (125 mg)	1	200	51	12.5	63.3	406.4
Cefixime + Ofloxacin (200 mg)	1	200	40	0.6	22.5	3650
Cefixime + Ornidazole (500 mg)	1	200	6	0.2	20.0	9900
Cefpodoxime + Clavulanate (125 mg)	1	200	32	21.0	39.0	85.71
Cefpodoxime + Ofloxacin (200 mg)	1	200	5	19.0	27.0	42.10

Relationship between percent price variation and number of manufacturing companies

When we draw a graph showing relationship between manufacturing companies and percent price variation, a peculiar relationship in between these two variables was noted. The number of manufacturing companies showing 0 - 100% price variation were considerably higher than 101-400% price variation range. Beyond this range, there exists a linear relationship. As the number of manufacturing companies increases, the percent price variation also increases (Figure 1).

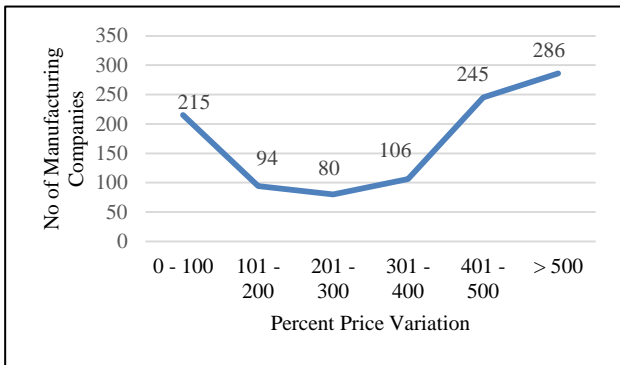


Figure 1: Relationship between percent variation and number of manufacturing companies.

DISCUSSION

It is evident from our study that there is a wide discrepancy in the price of oral cephalosporins in the Indian market. A varied number of pharmaceutical companies, ranging from 2 companies to 126 companies for a single drug, manufacture these drugs in varied formulations. Ideally, according to the current marketing strategies, as the number of companies manufacturing a particular formulation increases, the number of generic medicines available for the particular drug also increases. Thus, the percent price variation of that formulation should decrease proportionately. Figure 1 shows a peculiar aberration wherein the graph shows a decreasing trend in the initial price variation range and an increasing trend at higher range.

Furthermore, there are ample instances of studies done earlier, which show the wide price variation amongst different formulations of the same drugs. The evident wide variation in the oral anti-diabetic drugs, anti-hypertensives, anti-retrovirals and cephalosporins (antibiotics) has funded an intense debate over the possible reasons for this discrepancy.^{7-9,31}

One of the primary reasons for this price variation is the asymmetry of information or imperfect information amongst practitioners about price of a drug and the resultant expensive treatment.⁷⁻¹³ The cost of a drug is a major deciding factor for the patient’s compliance to treatment. In the World Health Organisation (WHO)

Guide to good prescribing, “P” stands for personal. It implies that a prescriber is entitled to select drugs on a rational basis, considering the efficacy, safety, suitability and cost of available drugs for a particular condition.¹⁴

Though a lot is known about efficacy, safety and suitability of drugs, the cost factor is often neglected and ignored. In the absence of knowledge on comparative prices, it is difficult for practitioners to prescribe the most economical treatment. Unaffordable treatment practice add up to the out-of-pocket expenditure.⁹ Antimicrobials like cephalosporins are one of the most frequently prescribed drugs with specific dosage schedule and duration.⁴⁻⁶ Complete resolution of the disease depends a lot on the patient compliance. The practitioners must be sensitized about the cost of therapy to ensure adequate patient compliance.⁹

Economic goals of the parent company and their targeted returns on the initial investment could lead to a significant rise in the price of the drug.⁷⁻¹³ The total average expected cost of developing a new drug would be \$ 802 million per new molecular entity.^{15,16} This would include costs of raw supplies, distribution and promotion of drugs, etc. Thus drug development is a high-risk, high-reward game; where the parent company, once the drugs go through, reaps in profits on the initial investment made. Such exuberant pricing should be avoided for the benefit of the general public and the company should undergo a proper study of the existing market structure of the region. Pricing strategies of a pharmaceutical industry shows a definite geographical variation.² There are two main pricing strategies which are in practice at present. First, penetration pricing strategy, wherein price of a new product does not differ from the existing drugs.² This is optimal in developed countries where there is greater product substitution.²

Skimming pricing strategy is optimal in developing countries where there is limited substitutability of therapeutic drugs.² Here, an initial high price for a new drug is set and it is lowered over time, as the product substitution becomes available.² Pharmaceutical companies practice this to cover high expenses related to investments and testing, and establish a patent over these branded medicines. To avoid this, generic medicines offer an affordable substitution to the branded medicines.³

Generic medicine is a copy of the original branded product, marketed after the expiry date of the patent or other exclusive rights.³ Hence, they are supposed to be of low cost. It contains the same drug in the same quantity as the brand medicine and are manufactured conforming to international standards.³ Emphasis should thus be on practising penetration pricing strategy with greater substitution for the branded medicines.

The government should also take proper responsibility to curtail the increasing price variations.⁷⁻¹³ Prior to 2005,

branded medicines were manufactured by multinational and large Indian pharmaceutical companies.³ As a result, the drugs were usually expensive. The Amendment of Indian Patent Act in 2005 resulted in growth of generic pharmaceutical industries thus making drugs available at low cost.^{3,18}

Strong measures are being taken by the union government and other regulatory bodies to check the doctor-pharmaceutical connection and unethical marketing practices. Through an authoritative decision dated January 21, 2013, Medical Council of India (MCI) has directed principals of medical colleges, directors of hospitals and presidents of all state medical councils that every physician should, rationally, as far as possible, prescribe drugs with generic names.^{3,17} So now, instead of the doctors, pharmaceuticals provide generic medicines to the pharmacies at lower maximum retail prices (MRPs) as decided by the government.^{3,17}

Also the Drug Price Control Order (DPCO) 2013 has been brought into effect from June 2013.¹⁹ This is an implementation by the National Pharmaceutical Pricing Authority (NPPA) to revise the price of formulations listed under National List of Essential Medicines (NLEM) 2011 to ensure affordability of essential medicines to the common people.^{19,20}

DPCO 2013 replaces DPCO 1995 which accounted for price regulation of 74 bulk drugs, while DPCO 2013 accounts for almost 628 drugs.^{19,21} This might come as a welcome respite, but many loopholes have been cited in the DPCO 2013.^{22,23} Some of them are:

- Only drugs on the NLEM will be included where the NLEM itself has been criticized for improper selection of drugs.^{22,24} Thus though certain cephalosporins (Cap Cefalexin 500 mg; Tab Cefixime 100 mg and 200 mg) have been included in the NLEM, others have been excluded.¹⁹ Nevertheless it is clear from our study that Cap Cefalexin 500 mg, Tab Cefixime 100 mg and Tab Cefixime 200 mg show a percent price variation of 693%, 410% and 81% respectively.
- Certain dosages and formulations are not yet included in the DPCO although the parent drug may be included in it. Manufacturers might take undue advantage of this fact and change the dosages and formulations to avoid the DPCO.^{19,22}
- "Market based pricing" has been used to determine the ceiling price.^{19,22} Wholesalers and retailers have faced a great loss as the margin of profit goes down resulting in lower sales. This has led to shortage of many life-saving medicines in the market.¹⁴

The Rashtriya Swasthya Bima Yojana (RSBY), literally "National Health Insurance Programme" has been started by the Government of India in 2008.^{22,25} The objective of this programme is to provide protection to the Below Poverty Line (BPL) households from financial liabilities

involving health scares involving hospitalization.²⁵ Beneficiaries are entitled to hospitalization coverage upto Rs. 30,000 through insurance companies (Ministry of Labour and Employment, 2013).²⁵

But, it does not cover the outpatient costs and the out-of-pocket expenditure.^{22,25} According to the National Sample Survey (NSS) for the year 1999-2000, in rural India, the share of drugs in the total Out-of-Pocket expenditure (OPP) was estimated to be nearly 83%, while in urban India, it was 77% (NPPP, 2011).^{20,22} Thus the coverage under RSBY is less desirable as many poor still remain uninsured. Another irony is that many villages do not even have hospitals to avail the schemes.

This remains a major drawback as, if more number of people get insured, their total medical expenses would be looked after by the insurance companies.²⁶ This would ensure a continuous consumption of medicines by the patients for their treatment. Thus, the pharmaceutical companies, wholesalers, retailers would not undergo major loss and their operating income margin would remain intact.

A limitation of the study would be that a cost effectiveness study done comparing the amount of drugs purchased by general public having different prices and the resultant effectiveness of the treatment modalities would give a better idea about the pharmaco-economic condition. Also parenteral formulations could be included in the study.

CONCLUSION

Exuberant pricing adds to the ever increasing economic burden on the general public. Thus the need of the hour is a joint cooperation from practitioners, pharmacists, regulatory authorities and the general public at large to take some action to reduce this price variation while maintaining the therapeutic efficacy. Practitioners must keep in mind the socio-economic background of the patients while prescribing lifesaving drugs like antimicrobials, anticancer drugs, etc.

Generic medicines must be preferentially prescribed as far as possible to control the expense. The government should make efforts to bring all the people under a standard health insurance programme which is relevant to urban as well as rural populations as a whole. Stringent government orders must be enforced and they should include all the pharmaceutical companies, retailers and wholesalers equally. Such measures will lead to consumers paying lower price for the drugs and increasing the consumption, thereby raising social welfare.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

- World Health Organisation. Factsheet: The 10 leading causes of death by country income group, 2012. Available at <http://www.who.int/mediacentre/factsheets/fs10/en/index1.html>. Accessed 12 July 2015.
- Caldera A, Zarnic Z. Affordability of Pharmaceutical Drugs in Developing Countries. *Advanced Studies in International Economic Policy Research*, Kiel Institute for World Economics. Working Paper 419. 2015:7.
- Pichholiya M, Basu A, Yadav AK, Kothari N, Tahashildar J. An observational comparative study of cost between branded medicines and generic medicines. *Int J Basic Clin Pharmacol.* 2015;4:269-72.
- Antibacterial Drugs. In Rang HP, Ritter JM, Flower RJ, Hendersen G (Eds). *Rang and Dale's Pharmacology*. Chapter 51. 8th Edition. Elsevier Ltd., 2014:631-2.
- Penicillins, Cephalosporins, and Other β -Lactam Antibiotics. In: Brunton LB, Lazo JS, Parker KL, eds. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*. Chapter 53. 12th ed. New York, NY: McGraw-Hill. 2011:741-8.
- Mendall LA, Wundrick RG. Chapter 153. Pneumonia. In Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL (Eds). *Harrison's Principles of Internal Medicine*, 19th Edition. New York: McGraw Hill. 2012:803-13.
- Date AP, Mahajan HM, Dashputra AV, Bhosale RR. Study of variation in price of various antidiabetic drugs available in Indian market. *Int J Basic Clin Pharmacol.* 2015;4(1):36-40.
- Karve AV, Chattar KB. Cost analysis study of oral antihypertensive agents available in Indian Market. *Int J Basic Clin Pharmacol.* 2014;3(3):479-84.
- Jadhav NB, Bhosale MS, Adhav CV. Cost analysis study of oral antidiabetic drugs available in Indian Market. *Int J Med Res Health Sci.* 2014;2(1):63-9.
- Sarkar PK. A rational drug policy. *Indian J Med Ethics.* 2004;12:30-5.
- Roy V, Rewari S. Ambiguous drug pricing: a physician's dilemma. *Indian J Pharmacol.* 1998;30(6):404-7.
- Wertheimer AI, Grumer SK. Overview of international pharmacy pricing. *Pharmacoeconomics.* 1992;2(6):449-55.
- Berki SE, Richards JW, Weeks HA. The mysteries of prescription pricing in retail pharmacies. *Med Care.* 1977;15(3):241-50.
- Chapter 2 Introduction to P-drugs. In: De Vries M., Henning RH, Hogerzeil HV, Fresle DA. *Guide to Good Prescribing – A Practical Manual*, World Health Organisation Action Programme on Essential Drugs Geneva. 1994:17-20.
- Di Masi JA, Hansen RW, Grabowski HG. The Price of Innovation: New Estimates of Drug Development Costs. *Journal of Health Economics.* 2003;22(2):151-85.
- Adams CP, Brantner VV. Estimating the Cost Of New Drug Development: Is It Really \$802 Million? *Health Affairs.* 2006;25(2):420-8.
- Mukherjee R. Prescribe generic drugs: MCI to doctors 2013. Available at articles.indiatimes.com/2013-01-27/india/36576717_1_generic-drugs-generic-medicines-generic-versions. Accessed 12 July 2015.
- The Patents (Amendment) Act 2005. Controller General of Patents Designs and Trade Marks, Department of Industrial Policy and Promotion, Ministry of Commerce and Industry available at http://www.ipindia.nic.in/IPActs_Rules/IPActs_Rules.htm as accessed on 12 July 2015.
- Compendium of Notified Ceiling Prices of Scheduled Drugs – 2015. National Pharmaceutical Pricing Authority (Ministry of Chemicals and Fertilizers, Government of India) February 2015. Available at www.nppaindia.nic.in. Accessed on 12 July 2015.
- NPPP (2011). National Pharmaceuticals Pricing Policy. Available at <http://pharmaceuticals.gov.in/mshT2810/FTY2.pdf>. Accessed 12 July 2015.
- Kumar V, Gupta NV, Kumar KA. A Comparison between old and latest systems in DPCO. *Int J Pharmacy and Pharmaceutical Sciences* 2014;6(2):19-20.
- Thakkar KB, Billa G. Light at the end of the tunnel?: The Great Indian Pharmacoeconomics story. *Front. Pharmacol.* 2013;4:153. doi: 10.3389/fphar.2013.00153.
- Rajagopal D. (2013). Drug price control order may not achieve much. *The Economic Times*. Available at http://articles.economictimes.indiatimes.com/2012-2010-03/news/34238918_1_drug-price-control-order-combination-drugs-drug-industry-executives. Accessed on 12 July 2015.
- Manikandan S, Gitanjali B. National list of essential medicines of India: the way forward. *J. Postgrad. Med.* 2013;58:68-72.
- Rashtriya Swasthya Bima Yojana. About RSBY: What is RSBY? 2008. Available at http://www.rsby.gov.in/about_rsby.aspx. Accessed 12 July 2015.
- First Post-India (2013, October 3). SC Raises Ceiling Price Question on New Drug Price Control Order. *First Post-India*. New Delhi. Available at: http://www.firstpost.com/india/sc-raises-ceiling-price-question-on-new-drug-price-control-order-1150829.html?utm_source=ref_article. Accessed on 12 July 2015.
- Das SC, Mandal M, Mandal SC. A critical study on availability and price variation between different brands: impact on access to medicines. *Indian J Pharm Sci.* 2007;69(1):160-3.
- Patel D, Thiyagu R, Surulivelrajan M, Patel H, Pandey S. Price variability among the oral antibiotics

- available in a South Indian Tertiary Care Hospital. *J Clin Diagn Res.* 2009;3(6):1871-5.
29. National List of Essential Medicines, 2011. Available from: <http://www.mohfw.nic.in/WriteReadData/1892s/7364497>. Accessed 12 July 2015.
30. World Health Organisation. Essential drugs and medicines: Drug finance. Available at: http://www.whoindia.org/EN/Section2/Section/Section160_959.html. Accessed 12 July 2015.
31. Panchal SS, Pandit PR, Phatak AM, Lohi KM. Cost analysis of antiretroviral agents available in India. *Int J Basic Clin Pharmacol.* 2015;4(3):479-82.

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