8 EXPERIMENTAL WORK

8.1 EVALUATION AND COMPARISON OF THE QUALITY & PRICING OF THE BRANDED / GENERICS, AS AVAILABLE FROM THE MARKET, FOR SELECTED CATEGORIES OF DRUGS.

The use of generic drugs is steadily increasing internationally as a result of economic pressure on drug budgets. Generic drugs provide the opportunity for major savings in healthcare expenditure since they are usually substantially lower in price than the innovator brands (King, 2002). However, physicians are apprehensive regarding the quality of generic drugs (Tilleyard, 1990; Biswas et al., 2000) and have concerns about reliability of generic drugs as well as generic interchange of certain drug categories (Hassali et al., 2010).

FDA recently evaluated 2,070 human studies conducted between 1996 and 2007. These studies compared the absorption of brand name and generic drugs in to a person’s body. These studies were submitted to FDA to support approval of generics. The average difference in absorption into the body between the generic and brand name was only 3.5% (Davit, 2009). Some generics were absorbed slightly more, some slightly less. This amount of difference would be expected and acceptable, whether for one batch of brand name drug tested against another batch of the same brand, or for a generic tested against a brand name. There have been studies in which branded drugs were compared with themselves as well as with a generic and results were similar.

Marketing practices adopted by manufacturers of imported branded medicines also propagate the belief that generics are of inferior quality as reported from countries in Central and Eastern Europe and independent countries emerged from former Soviet Union (Joncheere, 2003). The present study was conducted to compare the quality and price of generic (branded-generic) drug products to its expensive popular brand (branded) drug product manufactured by the same pharmaceutical company in India.

Currently, almost all medicines in India are sold under a brand (trade) name and medicines are called as branded medicines or branded-generic. In real sense Indian market does not have branded medicines (a name commonly given to an innovator product) because till January 2005, product patent was not applicable in India. In India, many pharmaceutical companies manufacture two types of products for the same
molecule, *i.e.*, **branded product** which they advertise and push through doctors and **branded-generic** which they expect retailers to push in the market. So called **branded medicines** in India are manufactured and promoted by multinationals or by reputed Indian manufacturers. **Branded-generics**, on the other hand, are not promoted or advertised by the manufacturer. This category closely resembles formulations referred to as ‘generics’ worldwide. Patients’ and doctors’ perception for all **branded-generics** irrespective of company is the same. All the strips and containers of the medicines are printed and labeled with MRP (maximum retail price) by the drug manufacturer in India as per the provision under Paragraph 14 of The Drug (Price Control) Order 1995. Medicines are available to patient at the MRP mentioned on the package of medicine (Shrank, 2009).

Detailed comparative evaluation studies on price and quality of commonly used branded versus branded-generic medicines of some selected categories manufactured by the same Indian manufacturer were carried out. The study was done with the objective to know if the quality of medicine is related to its price and also if branded product is better than its generic counterpart. Different categories of branded and generic medicines manufactured and marketed by same pharmaceutical company with different price tags were selected and subjected to comparative quality evaluation tests following the standards as provided under Indian Pharmacopoeia, 2007.

**SELECTION OF MEDICINES**

Branded and branded-generic versions of five commonly used medicines manufactured by the same pharmaceutical manufacturer (belonging to different therapeutic categories) were selected at random for the study. The five medicines chosen were: Alprazolam (0.25 mg), Cetirizine (10 mg), Ciprofloxacin (500 mg), Fluoxetine (20 mg), and Lansoprazole (30 mg). Branded and generic versions of same molecule manufactured by the same company were specifically selected for this study to know if the manufacturer makes any difference in their quality or follow similar statutory parameters.

**QUALITY TESTING**

The test samples were procured from the licensed authorized medicine dealers through valid purchase invoices. The sample size comprised 10x10 tablets/capsules of both **branded** and **branded-generic** version of each drug product. Efforts were made to procure these test samples (pair of the test sample) having almost identical dates of
manufacturing to rule out the possibility of difference in assay of the samples bearing different dates of manufacturing. The qualitative as well as quantitative analysis was carried out in a government approved laboratory following the methods (Annexure-I) prescribed in Indian Pharmacopoeia, 2007 as per their standards laid down in the Drugs and Cosmetics Act 1940 and Rules 1945 (Malik, 2010).

The following tests were performed:

- **Identification test:** Identity of the drug molecule was established by performing identification test through instrumental analysis using HPLC (high performance liquid chromatography) or IR (infra-red spectroscopy) following the method as prescribed.

- **Chemical composition test:** The samples were subjected to quantitative analysis using HPLC instrumental analytical methods as provided in Indian Pharmacopoeia 2007.

- **Uniformity of content test:** To confirm the uniformity of contents in the batch, the sampled dosage units were subjected to "uniformity of content" test wherein assay on 10 units of dosage form were performed individually using instrumental analytical methods. The test for uniformity of content is not applicable to tablets/capsules containing more than 10 mg; it was conducted only for Alprazolam (0.25 mg) and Cetirizine (10 mg) containing drug products.

- **Uniformity of weight:** All five pairs of samples were tested for uniformity of weight as prescribed.

- **Tests for Dissolution:** The samples were subjected to dissolution studies to evaluate their drug release pattern. These studies were performed in the dissolution media specified in the individual monograph of the Indian Pharmacopoeia 2007 on six dosage units and were indicative of the *in vivo* availability of active drug moiety from the dosage form, *i.e.*, tablet or capsule.

**RESULTS**

**Comparative price and mark-up for branded and branded generic pair of medicines**

Details of five ‘pair’ of medicines including their brand names as manufactured and sold in the Indian market, strength, dosage form, and the pharmaceutical company that
manufacture these products are given in Table 8.1.1. Price-to-patient (MRP) and price-to-retailer (PTR) for all the five ‘pair’ of medicines is also tabulated in Table 8.1.1. PTR for branded product of Cetirizine was 11 times more than the PTR of its counterpart branded-generic manufactured by the same company. Retailer was found having profit margin of INR 22.76 per 1x 10 tablets of branded-generic version in comparison to INR 8.16 for its branded version. The MRP printed on both the branded and branded-generic Ciprofloxacin tablets 500mg was found identical but the branded-generic was found sold to retailer at 3.6 times less than its branded counterpart.

Maximum Retail Price (MRP) printed/labeled on these branded medicines were 41%, 33%, 0%, 14%, and 31% higher than the Maximum Retail Price printed/labeled on their counterpart branded-generic versions manufactured by the same company. On the other hand, price-to-retailer (PTR’s) for branded-generic were found to be 1112%, 397%, 266%, 170%, and 439% less than their counterpart branded versions of Cetirizine, Fluoxetine, Ciprofloxacin, Lansoprazole, and Alprozolam formulations respectively. Retailer mark-ups for these five ‘pair’ of medicines i.e., branded vs. branded-generic: (Cetirizine, Fluoxetine, Ciprofloxacin, Lansoprazole, and Alprozolam were found to be 30% vs. 1016%, 25% vs. 367%, 25% vs. 357%, 27% vs. 201%, and 25% vs. 415% (Table 8.1.1). Similar findings have also been reported in daily newspaper with respect to huge profit margins about generic medicines (Sood, 2010).

The comparative price structure reveals that:

i) Branded medicines provide a mark-up of approximately 30% to the retailers.

ii) Branded-generics offer a very high mark-up (up to 1016%) for retailers.

Comparative evaluation of quality of branded and branded generic pair of medicines

- Identification test – All the five ‘paired’ medicines of branded and branded-generics gave positive identification tests when tested on HPLC or IR establishing their chemical identity (Table 8.1.2).

- Chemical composition test – The quantitative analysis conducted using HPLC method showed that each unit of the tested samples to be well within the prescribed range (Table 8.1.2).
• *Uniformity of content* – This test was done for Alprazolam tablets and Cetirizine tablets and results for both the versions of these medicines were within the prescribed range (Table 8.1.2).

• *Uniformity of weight* – Each sample of the five paired medicines was within prescribed limits (Table 8.1.2).

• *Dissolution test* – The dissolution test for all the five ‘paired’ medicines were within the permissible limits of the statutory standards (Table 8.1.2).

The comparative analytical studies revealed that both versions (branded and branded-generics) of the same molecule confirms to their statutory standards of quality and are alike as far as their quality is concerned.


No relation of any kind was found between the quality of the medicine and its corresponding price. The difference in the price structure of branded and branded-generic medicines was found attributed to the different marketing strategies adopted by their pharmaceutical companies. The price of medicines was found linked to their marketing strategies, wherein the products with popular brand name were found promoted by the drug companies through various means including incentives to the prescribing doctors. Branded-generics products, on the other hand were found sold without any sale promotional expenses on their marketing. Comparative results of these paired medicines are tabulated in Table 8.1.2. & Table 8.1.3.

In another similar study performed on different batches of branded as well as branded-generic versions of Alprazolam, tablets manufactured and marketed by the same pharmaceutical company in India, yielded similar results, when subjected to quality testing as per the mandatory pharmacopoeial standards. The comparative results of the said study are tabulated in Table 8.1.4.

DISCUSSION

Findings of the study revealed that pharmaceutical companies offer high mark-ups to the retailers on branded-generic medicines as compared to their branded counterparts. The profit margins to the retailers for five branded-generic medicines studied were in the range of 201-1016% as compared to the meager margins to the tune of 25-30% for their branded counterpart manufactured by the same company. Both versions of all five medicines cleared all the quantitative and qualitative parameters as prescribed in Indian Pharmacopoeia, 2007. These five ‘paired’ medicines were found identical in their quality and fulfilled all the criteria prescribed in their statutory standards. Similarly when five different batches of branded as well as branded generic Cetirizine tablets 10 mg manufactured and marketed by M/S Cipla were subjected to comparative quality evaluation tests as per mandatory pharmacopoeial standards, their quality were found alike (Pahwa, 2010).

The general notion and apprehensions about the quality of branded-generic version of the medicines vis-à-vis branded medicines prevalent among the healthcare providers, therefore appears to be a myth only. These paired branded and branded-generic medicines were manufactured by the same ‘reputed’ company using same manufacturing facilities and following GMP but yet these versions did not enjoy equality in the minds of physicians. There exists a widespread belief among the healthcare providers including doctors that the branded product is better in terms of quality and safety than its generic counterpart (Shafie et al., 2008; Figueiras et al., 2008; Kjøenniksen et al., 2006).

A systematic review and meta-analysis study evaluating the results of 38 published clinical trials that compared cardiovascular generic drugs to their branded counterpart revealed that there was no evidence that brand name heart drugs worked any better than generic heart drugs. This study concluded that there is no evidence of superiority of brand name to generic drugs (Kesselheim et al., 2008). Such studies may be helpful in promoting generic drug use that reduces unnecessary spending without improving clinical outcome. In most developed countries, generic medicines are promoted by competition-enhancing policies operating through health-care reimbursements to contain expenditure and encourage efficient use of resources (Kanavos et al., 2008). Generic substitution rates have increased remarkably in the US, probably due to greater acceptance of generics by physicians and pharmacists as well as encouragement from the third payers (Dong, 1999). Cheaper generics are one of the important factors to reduce healthcare cost. The practice
of generic substitution is strongly supported by health authorities in many developed countries (Smeaton, 2000). Use of generic drugs which are bio-equivalent to brand name drugs can help contain prescription drugs pending (Nightingale, 1998).

The term ‘generic drug’ has not been specifically defined under the Indian drug regulations. BA/BE studies for manufacturing/ marketing approval of generic medicines are not mandatory in India. There exist no generic promotion policies like mandatory generic prescription, provisions for generics substitution, identification mark on generics, lower price of generics etc. Although, there is independent central regulatory agency under the Ministry of Pharmaceuticals to regulate the availability and affordability of medicines in the country yet there are virtually no policies for generic promotion.

Majority of the medicines in India, are sold under a brand (trade) name and are termed as ‘branded medicines’. Generic medicines have been virtually vanished from the Indian market and are being replaced with branded-generics, which are simply generic medicines marketed under a brand name. Many pharmaceutical companies manufacture both the versions of same molecule, i.e., ‘branded’ which they promote and push through doctors and ‘branded-generic’ version, which they expect retailers to push in to the market. Access to the required medicines is still a burning issue in the country in spite of the fact that India is known as power house of cheaper medicines in the world.

Indian government must take up generic promotional schemes, general awareness programs on quality and efficacy of generics to build confidence among the prescribers, pharmacists and consumers. Studies involving comparative evaluation on quality of branded and their generic counterpart be made mandatory for the generic (or branded-generic) manufacturer and their reports should be made public to promote generic use and prescriptions. The generic substitution should be encouraged and be given the statutory force. Suitable changes in drug price policy may be made to have lower prices for branded-generic version of the therapeutic molecule. Transparency in fixing the maximum retail price by the manufacturer and clear guidelines for mark-ups at least for branded-generics is required in pharmaceutical trade. Availability of generics or branded-generics in the market with lower price tag is essential to make the medicines affordable. Along with consumer awareness, development and implementation of policies promoting generic use by health professionals and regulating mark-ups and medicine prices for generics could help ensure prescription and availability of affordable generics in India.
8.2 EVALUATION AND COMPARISON OF THE QUALITY & PRICING OF GENERICS, FROM JAN AUSHADHI STORES, WITH THEIR BRANDED COUNTERPARTS, FOR SELECTED CATEGORIES OF DRUGS.

With a view to adjudge and compare the quality of medicines available at Jan Aushadhi Stores with that of their counterpart branded medicines available in private sector, a comparative quality evaluation study was undertaken on four pairs of commonly used branded and Jan Aushadhi medicines. The branded medicines were purchased from the licensed medicine dealers while the Jan Aushadhi medicines were procured from Indian Drugs and Pharmaceutical Limited (IDPL) Gurgaon, one of the Public Sector Undertakings (CPSU's) catering these generic stores, for carrying out the studies. The medicines chosen were: Alprazolam 0.25 mg tablets, Cetirizine 10 mg tablets, Ciprofloxacin 500 mg tablets and Fluoxetine 20 mg capsules. The sample size comprised 10x10 tablets/capsules of both branded and branded-generic version of each drug product. Qualitative as well as quantitative analysis was carried out in a government approved testing laboratory following the methods (Annexure-I) prescribed in the Indian Pharmacopoeia, 2007 as per their standards laid down under the Drugs and Cosmetics Act 1940 and Rules 1945.

The following tests were performed:

- **Identification test:** Identity of the drug molecule was established by performing identification test through instrumental analysis using HPLC (high performance liquid chromatography) or IR (infra-red spectroscopy) following as prescribed for each medicine.

- **Chemical composition test:** The samples were subjected to quantitative analysis using HPLC instrumental analytical methods as provided in Indian Pharmacopoeia 2007.

- **Uniformity of content test:** To confirm the uniformity of content in the batch, the sampled dosage units were subjected to "uniformity of content" test wherein assay on 10 units of dosage form were performed individually using instrumental analytical methods. The test for uniformity of content is not applicable to tablets/capsules containing more than 10 mg; it was conducted only for Alprazolam tablets (0.25 mg) and Cetirizine tablets (10 mg).
Uniformity of weight: All four pairs of sample were tested for uniformity of weight as prescribed.

Tests for Dissolution: The samples were subjected to dissolution studies to evaluate their drug release pattern. These studies were performed in the dissolution media specified in the individual monograph of the Indian Pharmacopoeia 2007 on six dosage units and were indicative of the in vivo availability of active drug moiety from the dosage form, i.e., tablet or capsule.

RESULTS

Comparative evaluation of quality of paired medicines (Jan Aushadhi v/sbranded)

- Identification test – All the four ‘paired’ medicines of branded and Jan Aushadhi gave positive identification tests when tested on HPLC or IR establishing their chemical identity (Table 8.2.1).

- Chemical composition test – The quantitative analysis conducted using HPLC method showed that each unit of the tested samples to be well within the prescribed range (Table 8.2.1).

- Uniformity of content – This test was done for Alprazolam tablets and Cetirizine tablets and results for both the versions of medicines were within the prescribed range (Table 8.2.1).

- Uniformity of weight – Each unit of the sample was within prescribed range for all the four ‘pair’ of medicines (Table 8.2.1).

- Dissolution test – The dissolution test for all the four ‘paired’ medicines were within the permissible limits of the statutory standards (Table 8.2.1).

The study revealed that both versions (branded medicines and Jan Aushadhi medicines) of the same molecule conforms to their statutory standards of quality and are alike as for as their quality is concerned. The results of the studies are tabulated in Table 8.2.1.

DISCUSSION

Since the concept of 24x7 Jan Aushadhi Store is newer and novel in nature, the comparative quality evaluation studies of branded vis-à-vis Jan Aushadhi medicines has not been carried out so far in the country. This concept of providing generic medicines at lower printed MRP through these Jan Aushadhi Stores had been initiated by the Government of India after the commencement of this research project. Therefore it was thought prudent to under comparative quality evaluation studies of branded and their counterpart Jan Aushadhi medicines. This is the first such study conducted in India to systematically evaluate the quality of selected categories of medicines available at Jan Aushadhi Stores operational in the public facilities vis-a-vis their equivalent branded medicines available in the market. To start with, the study was limited to only four medicines and it is required to be expanded further on the left out medicines to draw concrete conclusion about the quality of medicines available at Jan Aushadhi Stores. Further such studies are also important from the point of view to instill faith about their quality and efficacy of these medicines in the minds of consumers as well as prescribers.

CONCLUSION

The study revealed that the medicines available at Jan Aushadhi Stores are of equivalent and comparable quality with the quality of costlier branded medicines available in the market. The government should, therefore, expand the scheme of opening such stores throughout the country to provide quality medicines at affordable prices to the larger section of its population. There is also dire necessity of expanding the scope of the study to the entire range of medicines available at generic stores. Creating public awareness by advertisements in print as well as electronic media to instill confidence in the minds of patients and physician regarding the quality and efficacy of such drugs and also to propagate that patient asked their doctors to prescribe medicines carrying the scheme’s logo, retailers would have no choice but to stock them.