Chapter 3

Pharmacopoeial Evaluation of 50 mg Immediate Release Marketed Metoprolol Tartrate Tablets ...
1. INTRODUCTION

The most significant impediments to keeping patients healthy and curing disease is noncompliance with prescribed medication regimens\(^1\), especially in long-term continual therapy\(^2,3\). From our study carried out for people suffering from hypertension, Chapter 2 of this thesis, it was found that 38.85% (±1.35) population was skipping their dose deliberately for high cost of medicines; only ~40% male and ~26% females were regularly taking medicines. With rising healthcare cost, Indian government is putting efforts to favor the prescription of generic drugs and it is expected that drugs worth US $ 31 billion is to face patent expiry in years leading to 2010\(^4\).

Generic drug products are considered to be cheap therapeutically equivalent to the brand name product whose patents have been expired\(^5,6\). The topic has been dealt in detail, in Chapter 1.

3.2. OBJECTIVE

3.2.1. To comparatively evaluate 50 mg immediate release (IR) metoprolol tartrate tablets from different manufacturers available in the Indian market to USP 27 NF 22 specifications.

3.2.2. To estimate the projected, cost of the drug therapy for each product for one year based on the usual dosage regimen.

3.3. EXPERIMENTAL STUDIES

3.3.1. DOSAGE FORM CHARACTERIZATION - UNOFFICIAL TESTS

3.3.1.i. Organoleptic Properties

Shape & Color: Visual inspection under magnifying glass.
Size determination: Digimatic Micrometer, Mitutoyo, Japan, with ± 0.001mm accuracy.

3.3.1.ii. Test for Friability

Equipment: Electrolab EF-2 Friabilator, USP, Mumbai.
Tablet Quantity: ~7 gms of tablets.
Tolerance: Not more than 1% after 100 revolutions.

3.3.1.iii. Crushing strength (Hardness Test)

Equipment: Tablet Hardness Tester, Pfizer Type (with 0.1 kg accuracy).
Number of Units: 6 (Average value)

3.3.2. OFFICIAL TESTS AND SPECIFICATIONS

3.3.2.1. Test for Weight Variation

Equipment: Precisa XB 220 A (with 0.0001 gm accuracy).
Number of Units Weighed: 10.
Tolerance: Amount of the active ingredient in each of the 10 dosage units lies within the range of 85.0% to 115.0% of the label claim assuming homogeneous distribution of the active ingredient; and the relative standard deviation is less than or equal to 6.0%.

3.3.2.ii. Test for Drug Content Uniformity

Equipment: Pharma Spec UV1700 UV Visible Spectrophotometer, Japan.
Number of Units Assayed: 10.
Assay: UV Spectrophotometric at 275 nm in distilled water.
3.3.2.iii. Disintegration

Equipment: Electrolab ED-2 Disintegration Tester, USP, Mumbai.
Number of Units: 06.
Medium: 1000 mL Distilled water.
Temperature: 37 °C (± 2).
Tolerance: No part of the tablet retained on the screen; if, then the residual mass is not palpable.

3.3.2.iv. Dissolution Test Conditions

Equipment: Electrolab TDT-08L Dissolution Tester, USP, Mumbai.
Number of units to be tested: 06.
Medium: Simulated gastric fluid (without enzyme; 900 mL).
Apparatus 1: 100 rpm maintained at 37 °C (± 0.5).
Time: 30 mins.
Tolerance: Not less than 75% (Q) of the labeled amount of drug dissolved in 30 mins.

3.4. PRODUCTS

The following products with their batch details were used in the study.

3.4.1. Betoloc® 50

Rx Metoprolol Tartrate Tablets IP
Each uncoated tablet contains Metoprolol Tartrate IP 50 mg.
Dosage: As directed by the Physician.
Precaution: Schedule H drug.
Warning: To be sold by retail on the prescription of a Registered Medical Practitioner only.
3.4.2. Lopressor® 50

Rₙ Metoprolol Tartrate Tablets IP

Each uncoated tablet contains Metoprolol Tartrate IP 50 mg.

Dosage: As directed by the Physician.

Precaution: Schedule H drug.

Warning: To be sold by retail on the prescription of a Registered Medical Practitioner only.

Storage: Protect from light.

Manufacturing License Number: PD-132.

Batch Number: 43002V

Manufacturing date: May 2004

Expiry date: Apr. 2008

Retail Price: Not to exceed Rs. 24.50 for 10 tablets. Local Taxes Extra.

Manufactured by: Emcure Pharmaceutical Ltd., C-10(12), FunctionalElectronic Estate, M. I D.C., Bhosari, Pune 411 026, India.

3.4.3. Metapro™ - 50

Rₙ Metoprolol Tartrate Tablets IP

Each uncoated tablet contains Metoprolol Tartrate IP 50 mg.

Dosage: As directed by the Physician.

Precaution: Schedule H drug.

Warning: To be sold by retail on the prescription of a Registered Medical Practitioner only.

Storage: Keep in a cool dry place.

Manufacturing License Number: 300

Batch Number: MTP-008

Manufacturing date: Oct. 2003

Expiry date: Sep. 2005

Retail Price: Not to exceed Rs. 17.00 for 10 tablets. Local Taxes Extra.

Manufactured by: MICRO LABS LIMITED, 92, SIPCOT Industrial Complex, HOSUR – 635120 (T.N.)
4.4. METO – 50

Metoprolol Tartrate Tablets IP

Each uncoated tablet contains Metoprolol Tartrate IP equivalent to 50 mg. 
Dosage: As directed by the Physician.
Precaution: Schedule H drug.
Warning: To be sold by retail on the prescription of a Registered Medical Practitioner only.
Storage: Protect from light.
Manufacturing License Number: 1488 A
Batch Number: MOB 103
Manufacturing date: Jan. 2003
Expiry date: Dec. 2006
Retail Price: Not to exceed Rs. 18.40 for 10 tablets. Local Taxes extra.
Manufactured by: Biotrans Pharmaceutical Pvt. Ltd., 3 New Natara- puram, 2nd 
Street, M.M.D.A. colony, Anumbakkam, Chennai – 600 106
Marketed by: Mano Pharmaceuticals Pvt. Ltd., 447, poonamallee, High 
Road, Chennai – 600 029.

3.4.5. Metolar - 50

Metoprolol Tartrate Tablets IP

Each uncoated tablet contains Metoprolol Tartrate IP 50 mg.
Precaution: Schedule H drug.
Warning: To be sold by retail on the prescription of a Registered Medical Practitioner only.
Manufacturing License Number: 366
Batch Number: T40171
Manufacturing date: Jun. 04
Expiry date: May 07
Retail Price: Not to exceed Rs. 20.50 for 10 tablets. Local Taxes Extra.
Manufactured by: MEDITAB SPECIALITIES PVT. LTD, 352 Kundaim Indl 
EstateGoa 403 115 Under the technical guidance of CIPLA LTD.

3.5. RESULTS AND DISCUSSION

3.5.1. Unofficial Tests

Two of the five products were blister form while others opted for strip packed. All the five products were uncoated, circular in color, colorless, but carried distinction/identification in terms of presence or absence of (i) beveled edges, (ii) engraved symbols, (iii) flat/convex surface and (iv) scored. Out of 5 products, 3 products were with ~0.8 cm in diameter and ~0.33 cm thickness but the maximum diameter of the tablet was ~0.9 cm with maximum thickness of ~0.35 cm. The
Fracture ability values for all the tablets was less than 1% while the hardness/crushing strength values varied from 0.53 to 5.57 kg/cm². The details of which are given in Table 3.1. and 3.2.

### Table 3.1
Packaging properties and appearance of various marketed 50 mg IR release metoprolol tartrate tablet.

<table>
<thead>
<tr>
<th>Product</th>
<th>Packaging</th>
<th>Appearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>IR-B</td>
<td>Strip</td>
<td>Uncoated, white, circular, biconvex, scored on one side with engraved symbols ‘H’ &amp; ‘M’ on same side. On the other side engraved with symbol ‘CG’.</td>
</tr>
<tr>
<td>IR-C</td>
<td>Strip</td>
<td>Uncoated, white, circular, flat with beveled edges at top and bottom.</td>
</tr>
<tr>
<td>IR-D</td>
<td>Blister</td>
<td>Uncoated, white, circular, flat with one surface beveled edged.</td>
</tr>
<tr>
<td>IR-E</td>
<td>Strip</td>
<td>Uncoated, white, circular, biconvex, scored on one side with beveled edges &amp; engraved on the other side engraved with symbol ‘MT’.</td>
</tr>
</tbody>
</table>

### Table 3.2.
Dimensional size, hardness and friability values in various marketed 50 mg IR metoprolol tartrate tablet.

<table>
<thead>
<tr>
<th>Product</th>
<th>Dimension</th>
<th>Hardness (kg/cm²)</th>
<th>Friability (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diameter</td>
<td>Thickness</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(cm)</td>
<td>(cm)</td>
<td></td>
</tr>
<tr>
<td>IR-A</td>
<td>0.807</td>
<td>0.325</td>
<td>5.57 (0.56)</td>
</tr>
<tr>
<td>IR-B</td>
<td>0.910</td>
<td>0.357</td>
<td>5.60 (1.17)</td>
</tr>
<tr>
<td>IR-C</td>
<td>0.800</td>
<td>0.268</td>
<td>5.12 (1.50)</td>
</tr>
<tr>
<td>IR-D</td>
<td>0.888</td>
<td>0.338</td>
<td>0.53 (0.05)</td>
</tr>
<tr>
<td>IR-E</td>
<td>0.800</td>
<td>0.263</td>
<td>1.68 (0.19)</td>
</tr>
</tbody>
</table>

* Values in the parenthesis indicate the standard deviation estimated from 6 separate tablets.
3.2. Official Tests And Specifications

All the marketed products of metoprolol tartrate qualified the official tests with the values within the specified limits. The values are given in Table 3.3. and fig. 3.1, 3.2, 3.3 and 3.4; which are self-explanatory. A close look at the data and the respective graphs indicate that all the tablets weight were highly consistent but was not so in IR-D coded tablet; so also the values in content uniformity test. The disintegration values were very much consistent in products coded IR-A, IR-B and IR-C, while for the amount of drug released at the end of 30 minutes were highly consistent for all the coded product except IR-C.

Table 3.3. Various official test result data on different marketed 50 mg immediate release metoprolol tartrate tablet.

<table>
<thead>
<tr>
<th>Product</th>
<th>Weight Variation (% Active Content)</th>
<th>Content Uniformity (Actual % Active Content)</th>
<th>Disintegration Test (mins)</th>
<th>Drug Dissolved at $T_{30}$ (min) (% Q)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IR-A</td>
<td>110.04 (1.26) a</td>
<td>110.04 (1.75) a</td>
<td>11.50 (0.11) b</td>
<td>109.68 (1.44) b</td>
</tr>
<tr>
<td>IR-B</td>
<td>110.04 (0.81) a</td>
<td>110.04 (1.17) a</td>
<td>9.23 (0.05) b</td>
<td>109.85 (0.79) b</td>
</tr>
<tr>
<td>IR-C</td>
<td>109.44 (3.06) a</td>
<td>109.57 (3.24) a</td>
<td>5.23 (0.11) b</td>
<td>109.14 (3.51) b</td>
</tr>
<tr>
<td>IR-D</td>
<td>110.85 (1.072) a</td>
<td>110.85 (3.26) a</td>
<td>1.51 (0.20) b</td>
<td>110.42 (1.07) b</td>
</tr>
<tr>
<td>IR-E</td>
<td>109.42 (109.42) a</td>
<td>109.42 (1.96) a</td>
<td>6.41 (0.35) b</td>
<td>109.19 (1.63) b</td>
</tr>
</tbody>
</table>

* Values in the parenthesis indicate the standard deviation estimated on a 10 and b 6 separate tablets respectively.
Fig. 3.1. Weight variation test values for the marketed product.

Fig. 3.2. Content uniformity test values for marketed product.
Fig. 3.3. Disintegration test value for marketed product.

Fig. 3.4. In vitro dissolution test at $T_{30}$ for marketed product.
Table 3.4. Cost of different marketed IR 50 mg marketed metoprolol tartrate tablet.

<table>
<thead>
<tr>
<th>Product</th>
<th>Cost for 10 Tablets (in Rupees)</th>
<th>Cost for 1 year (in Rupees)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Once/Day</td>
<td>Twice/Day</td>
</tr>
<tr>
<td>IR-A</td>
<td>23.53 (38.15%)</td>
<td>858.85 (238.35)</td>
</tr>
<tr>
<td>IR-B</td>
<td>24.50 (44.12%)</td>
<td>894.25 (273.75)</td>
</tr>
<tr>
<td>IR-C</td>
<td>17.00 (0%)</td>
<td>620.50 (0)</td>
</tr>
<tr>
<td>IR-D</td>
<td>18.40 (08.24%)</td>
<td>671.60 (051.10)</td>
</tr>
<tr>
<td>IR-E</td>
<td>20.50 (20.59%)</td>
<td>748.25 (127.75)</td>
</tr>
</tbody>
</table>

* Values in the parenthesis indicate the difference in cost from the lowest priced product.

Fig. 3.5. Estimated cost projection in different marketed IR 50 mg metoprolol tartrate tablet.
Cost Evaluation

Lifestyle drugs like metoprolol tartrate and other hypertensive drugs are generally prescribed once or twice in a day. Hence, the cost projection incurred by the patient for 1 year when taken once/twice a day are estimated in all the five marketed products. The data is given in table 3.4. (fig.3.5). The product cost found in increasing prices is: IR-C < IR-D < IR-E < IR-A < IR-B. When the cost difference in % was estimated, a difference of ~ 44% was found between the cheapest and the costliest product.
References


