The results were reproducible, even on tablets after storage indicated by standard deviation (Table 2).

Propranolol hydrochloride release from tablets was studied in acidic (pH 1.2 buffer) and alkaline (pH 7.5 buffer) solutions for a period of 12 h as prescribed for propranolol hydrochloride extended release capsules (test 2) in USP 24. The drug releases were well within limits (Table 3). Release followed near zero order kinetics after a lag period of 2 h ($R^2 = 0.95$). These data observed for two samples after 60 d of storage are shown as a function of time in fig. 1. The release appears to occur in three stages. An initial rapid release occurs for first 2 h, followed by a slow release that is almost linear in line. In the final stage, release slows further, tending to the almost saturation concentration of the drug. The in vitro release was extended over a period of more than 12 h. These results reveal that HPMC matrix tablet is useful for making an effective sustained release dosage form to achieve a desired release. It may be concluded that matrix system using suitable grade of HPMC polymer is a suitable delivery system for propranolol hydrochloride and can help to reduce dose of drug and frequency (twice daily).

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Synthesis and Antimicrobial Screening of Novel Mannich Bases of Isatin Derivative

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A new series of N-Mannich bases (Ia-Ih) of 3-semicarbazino isatin (I) was synthesized by reacting (I) with formaldehyde and various aromatic primary amines. The chemical structures were confirmed by means of IR, $^1$H NMR and elemental analysis. The compounds synthesized were screened for antimicrobial activity against Staphylococcus aureus, Escherichia coli and Candida albicans by

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cup plate method. All the compounds showed remarkable antimicrobial activity except compound Ia that showed moderate activity against *S. aureus*.

Isatin is an endogenous compound isolated in 1988 and reported to possess a wide range of central nervous system activities. Isatin is the biologically active chemical produced by an *Alteromonas* sp. strain inhabiting the surface of embryos of the cardian shrimp *Palaemon macrodactylus*, which protects them from the pathogenic fungus *Legionidium callinectes*. Schiff bases and Mannich bases of isatin were reported to possess antibacterial, antifungal, antiviral, antiprotozoal and antihelminthic activities. The good biological profile of isatin derivatives prompted us to synthesize some Mannich bases of 3-semicarbazino isatin and evaluate their antimicrobial activity. The title compounds were synthesized by reacting 3-semicarbazino isatin (I) with formaldehyde and various aromatic primary amines (Scheme 1). Elemental analysis, IR and $^1$H NMR spectra characterized the constitutions of synthesized compounds.

Melting points are uncorrected and were recorded in liquid paraffin bath using open-end capillaries. Thin layer chromatography was performed on silica gel-G plates and spots were visualized by using iodine vapors. $^1$H NMR spectra were recorded on a Bruker 300 MHz NMR spectrophotometer (internal reference TMS). The IR spectra were recorded on a Perkin Elmer spectrophotometer. Elemental analysis was performed on Carlo Erba 1108 analyzer.

3-Semicarbazino isatin (I) was prepared by taking equimolar quantities of isatin and semicarbazide in ethanol. The mixture was stirred for 4 h. The crude compound was filtered at pump and recrystallized from methanol, mp: 266-267°C; IR (KBr) cm$^{-1}$: 3422, 3350, 3167 (N-H), 1724, 1698 (C=O), 1609 (C=N), 1453 (C=C); $^1$H NMR (CDCl$_3$, DMSO-d$_6$)δ ppm: 6.72 (s, 1H, NH), 6.92 (d, 1H, Ar-H), 7.03 (t, 1H, Ar-H), 7.34 (t, 1H, Ar-H), 8.04 (d, 1H, Ar-H), 10.51 (s, 1H, NH), 11.73 (s, 2H, NH).

The compound 1-(4'-ethoxyanilinomethyl)-3-semicarbazino isatin (Ia) was synthesized by placing equimolar quantities of compound (I), phenetidine and formaldehyde in absolute ethanol. The reaction mixture was made acidic by adding few drops of glacial acetic acid and refluxed for 6 h on a water bath. After completion of reaction, the solution was concentrated to half of its volume and cooled. The crude product obtained was filtered and recrystallized from ethanol. IR (KBr) cm$^{-1}$: 3415, 3302, 3237 (N-H), 1720, 1700 (C=O), 1685 (C=N), 1620 (C=C); $^1$H NMR (CDCl$_3$, DMSO-d$_6$)δ ppm: 1.53 (t, 3H, -CH$_3$), 2.492 (d, 2H, N-CH$_2$), 4.91 (q, 2H, -CH$_2$), 7.07 (s, 6H, Ar-H), 7.11 (s, 2H, Ar-H), 7.59 (t, 1H, -NH), 11.10 (s, 1H, -NH), 11.71 (s, 2H, -NH$_2$); Anal. (C$_{18}$H$_{19}$N$_5$O$_5$) Found: C, 61.17%; H, 5.36%; N, 19.82%; Calculated: C, 61.18%; H, 5.38%; N, 19.83%. Similarly compound Ib-Ih were prepared.

![Scheme 1: Synthesis of title compounds](image)
2.499 (d 2H, -CH₂), 7.06 (t, 6H, Ar-H), 7.31 (t, 2H, Ar-H), 7.59 (s 1H, -NH), 11.72 (s, 2H, -NH₂);
Anal. (C₁₅H₁₄N₂O₂Cl) Found: C, 55.96%; H, 4.08%; N, 20.39%;
Calculated: C, 55.97%; H, 4.08%; N, 20.40%.

1-(4′-Bromonilinomethyl)-3-semicarbazino isatin (Ic): IR (KBr) cm⁻¹: 3475, 3312, 3230 (N-H), 1705, 1690 (C=O), 1675 (C=N), 1655 (C=C); ¹H NMR (CDCl₃, DMSO-d₆) δ ppm: 2.487 (d, 2H, -CH₂), 7.10 (t, 6H, Ar-H), 7.21 (t, 2H, Ar-H), 7.45 (t, 1H, -NH), 11.00 (s, 1H, -NH), 11.70 (s, 2H, -NH₂);
Anal. (C₁₇H₁₆N₂O₂Br) Found: C, 49.48%; H, 3.59%; N, 18.04%; Calculated: C, 49.48%; H, 3.60%; N, 18.04%.

1-(4′-Fluorooxilinomethyl)-3-semicarbazino isatin (Id): IR (KBr) cm⁻¹: 3420, 3396, 3253 (N-H), 1715, 1682 (C=O), 1650 (C=N), 1595 (C=C); ¹H NMR (CDCl₃, DMSO-d₆) δ ppm: 2.50 (d, 2H, -CH₂), 6.62 (d, 4H, Ar-H), 6.92 (d, 4H, Ar-H), 7.59 (t, 1H, -NH), 11.04 (s, 1H, -NH), 11.55 (s, 2H, -NH₂);
Anal. (C₁₅H₁₄N₂O₂F) Found: C, 58.71%; H, 4.27%; N, 21.40%; Calculated: C, 58.71%; H, 4.28%; N, 21.40%.

1-(4′-Aminopyridinomethyl)-3-semicarbazino isatin (Ie): IR (KBr) cm⁻¹: 3469, 3303, 3235 (N-H), 1706, 1685 (C=O), 1624 (C=N), 1575 (C=C); ¹H NMR (CDCl₃, DMSO-d₆) δ ppm: 2.5 (d, 2H, -CH₂), 6.15 (d, 1H, Ar-H), 7.09 (t, 4H, Ar-H), 7.30 (t, 1H, Ar-H), 7.59 (t, 3H, Ar-H, NH), 11.11 (s, 1H, -NH), 11.72 (s, 2H, NH₂);
Anal. (C₁₅H₁₄N₂O₂) Found: C, 58.05%; H, 4.51%; N, 27.07%; Calculated: C, 58.06%; H, 4.51%; N, 27.09%.

1-(4′-Nitroanilinomethyl)-3-semicarbazino isatin (If): IR (KBr) cm⁻¹: 3460, 3300, 3210 (N-H), 1700, 1690 (C=O), 1655 (C=N), 1630 (C=C); ¹H NMR (CDCl₃, DMSO-d₆) δ ppm: 2.50 (d, 2H, -CH₂), 7.05 (t, 6H, Ar-H), 7.27 (t, 2H, Ar-H), 7.56 (t, 1H, -NH), 11.12 (s, 1H, -NH), 11.55 (s, 2H, -NH₂);
Anal. (C₁₅H₁₄N₂O₂) Found: C, 54.23%; H, 3.94%; N, 23.71%; Calculated: C, 54.23%; H, 3.95%; N, 23.72%.

1-(4′-Methoxyanilinomethyl)-3-semicarbazino isatin (Ig): IR (KBr) cm⁻¹: 3469, 3350, 3239 (N-H), 1715, 1690 (C=O), 1613 (C=N), 1590 (C=C); ¹H NMR (CDCl₃, DMSO-d₆) δ ppm: 2.50 (d, 2H, -CH₂), 3.68 (s, 3H, -OCH₃), 7.08 (q, 4H, Ar-H), 7.31 (t, 3H, -NH, Ar-H), 7.59 (d, 2H, Ar-H), 11.15 (s, 1H, -NH), 11.75 (d, 2H, -NH₂);
Anal. (C₁₅H₁₄N₂O₂) Found: C, 60.16%; H, 4.99%; N, 20.62%; Calculated: C, 60.17%; H, 5.01%; N, 20.64%.

1-(3′-Aminopyridinomethyl)-3-semicarbazino isatin (Ih): IR (KBr) cm⁻¹: 3415, 3330, 3260 (N-H), 1710, 1695 (C=O), 1670 (C=N), 1590 (C=C); ¹H NMR (CDCl₃, DMSO-d₆) δ ppm: 2.49 (d, 2H, -CH₂), 7.16 (d, 5H, Ar-H), 7.41 (d, 2H, Ar-H), 7.65 (d, 1H, N-CH₂), 7.82 (t, 1H, -NH), 10.96 (s, 1H, -NH), 11.70 (s, 2H, -NH₂);
Anal. (C₁₅H₁₄N₂O₂) Found: C, 58.05%; H, 4.51%; N, 27.08%; Calculated: C, 58.06%; H, 4.51%; N, 27.09%. The physical data of these compounds are given in Table 1.

The in vitro antifungal and antibacterial activity was carried out against 24 h old cultures of two bacteria and one fungus by cup plate method. The bacteria used were S. aureus (NCTC 10418) and E. coli (NCTC 6571) and fungus used was Candida albicans. The compounds were tested at a concentration of 100 µg/ml in DMF solution using amikacin (100 µg/ml) and fluconazole (100 µg/ml) as the reference standard for comparison of antibacterial and antifungal activity.

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>Ar</th>
<th>Mol. Form.</th>
<th>Rₖ Value</th>
<th>mp (°)</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>la</td>
<td>4′-ethoxyphenyl</td>
<td>C₁₅H₁₄N₂O₂</td>
<td>0.78</td>
<td>234</td>
<td>63</td>
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<tr>
<td>lb</td>
<td>4′-chlorophenyl</td>
<td>C₁₅H₁₄N₂O₂Cl</td>
<td>0.61</td>
<td>242</td>
<td>79</td>
</tr>
<tr>
<td>lc</td>
<td>4′-bromophenyl</td>
<td>C₁₅H₁₄N₂O₂Br</td>
<td>0.73</td>
<td>176</td>
<td>45</td>
</tr>
<tr>
<td>ld</td>
<td>4′-fluorophenyl</td>
<td>C₁₅H₁₄N₂O₂F</td>
<td>0.48</td>
<td>184</td>
<td>76</td>
</tr>
<tr>
<td>le</td>
<td>Pyridine-4′-yl</td>
<td>C₁₅H₁₄N₂O₂</td>
<td>0.60</td>
<td>238</td>
<td>37</td>
</tr>
<tr>
<td>lf</td>
<td>4′-nitrophenyl</td>
<td>C₁₅H₁₄N₂O₂</td>
<td>0.65</td>
<td>252</td>
<td>79</td>
</tr>
<tr>
<td>lg</td>
<td>3′-methoxyphenyl</td>
<td>C₁₅H₁₄N₂O₂</td>
<td>0.77</td>
<td>78</td>
<td>52</td>
</tr>
<tr>
<td>lh</td>
<td>Pyridine-3′-yl</td>
<td>C₁₅H₁₄N₂O₂</td>
<td>0.55</td>
<td>170</td>
<td>49</td>
</tr>
</tbody>
</table>

All the compounds gave satisfactory elemental analysis with in ±0.4% of the theoretical values; Rₖ values were determined in benzene:acetone (8:2).

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<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>E. coli</th>
<th>S. aureus</th>
<th>Candida albicans</th>
</tr>
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<tr>
<td></td>
<td>Zone of inhibition (mm)*</td>
<td>% activity compared to standard</td>
<td>Zone of inhibition (mm)*</td>
</tr>
<tr>
<td>la</td>
<td>21</td>
<td>91.30</td>
<td>20</td>
</tr>
<tr>
<td>lb</td>
<td>19</td>
<td>82.60</td>
<td>16</td>
</tr>
<tr>
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<td>21</td>
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<td>ld</td>
<td>17</td>
<td>73.91</td>
<td>23</td>
</tr>
<tr>
<td>le</td>
<td>19</td>
<td>82.60</td>
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<tr>
<td>Amikacin</td>
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</tr>
<tr>
<td>Fluconazole</td>
<td>-</td>
<td>-</td>
<td>26</td>
</tr>
</tbody>
</table>

Solvent used is dimethyl formamide (No zone of inhibition), *Average of three independent determinations, Sabouraud dextrose agar media was used for antifungal activity.

tifungal activity respectively. Inhibition was recorded by measuring the diameter of the inhibition zone at the end of 24 h for bacteria and 48 h for fungus. Each experiment was repeated thrice and average of three independent determinations was recorded. The results of anti microbial activity are summarized in Table 2.

According to the antimicrobial screening by cup plate method, compounds la, ld, and le with p-ethoxyphenyl, p-fluorophenyl and pyridine-3'-yl group, respectively, exhibited most significant activity against S. aureus and C. albicans. Compound lf having p-nitrophenyl group showed most significant activity against C. albicans but moderate activity against S. aureus. Compounds la, lb, lc and le with p-ethoxyphenyl, p-chlorophenyl, p-bromophenyl and pyridine-4'-yl group, respectively, exhibited very good activity against E. coli while compound lg having 3'-methoxyphenyl group showed moderate activity against E. coli. Compound le with pyridine-4'-yl group exhibited better antimicrobial activity against E. coli as compared to compound lh having pyridine-3'-yl group. Presence of these two groups exhibited comparable antimicrobial against S. aureus and C. albicans. Substitution at the para position of phenyl ring exhibited decrease in antimicrobial activity as; p-ethoxy > p-chloro, p-bromo > p-nitro > p-fluoro against E. coli; p-fluoro > p-bromo > p-ethoxy > p-chloro > p-nitro against S. aureus and p-nitro, p-ethoxy >p-fluoro > p-bromo > p-chloro against C. albicans.

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Antifertility Activity of Ethanol Extract of Aristalochia tagala Leaf

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Ethanol extract of the plant Aristalochia tagala Cham. (Fam: Aristalochiaceae) was investigated for antifertility activity in female Wistar rats. Rats treated with the plant extract showed reduction in the number of corpora lutea and implantation sites. The extract exhibited significant activity (72%) on oral administration of 100 mg/kg and 100% activity at a dose of 200 mg/kg.

Rapid population growth has caused serious problem in economic growth and human development in the developing countries. The control of human fertility, in the sense of its limitation, is the most important and urgent of all bi-social and medicinal problems confronting mankind today. One approach being pursued to identify new antifertility agents is the search for their presence in natural sources. Many plant preparations are reported for their fertility regulating properties in the ancient Indian literature. Chaudhary and Haq, Kamboj and Dhawan have exhaustively reviewed research on Indian plants with antifertility activity.

Aristolochia, a large genus of shrubs, rhizomatous perennial herbs often twining, is distributed in tropical and temperate regions of the world. Of twenty species known extensive work has been carried out only on some of them like, Aristalochia indica, Aristalochia bracteolata and Aristalochia tagala, which are of much medicinal importance. These plants contain alkaloids and they have been used as a remedy for snakebite. Aristalochia tagala is a perennial herb highly prevalent in Himalayas, Bihar, Assam and southwards in forest clearings. The root of the plant is reported to contain aristolochic acid, which possesses tumor-inhibiting activity and has been used in the treatment of cancer, snakebite, and helminthiasis.

It is reported that root extracts of Aristalochia tagala are used in female antifertility, as a tonic or emmenagogue and in the treatment of bowel complaints. Literature survey revealed that no work was carried out on the leaves of

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