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 If that showed moderate activity against *S. aureus*.

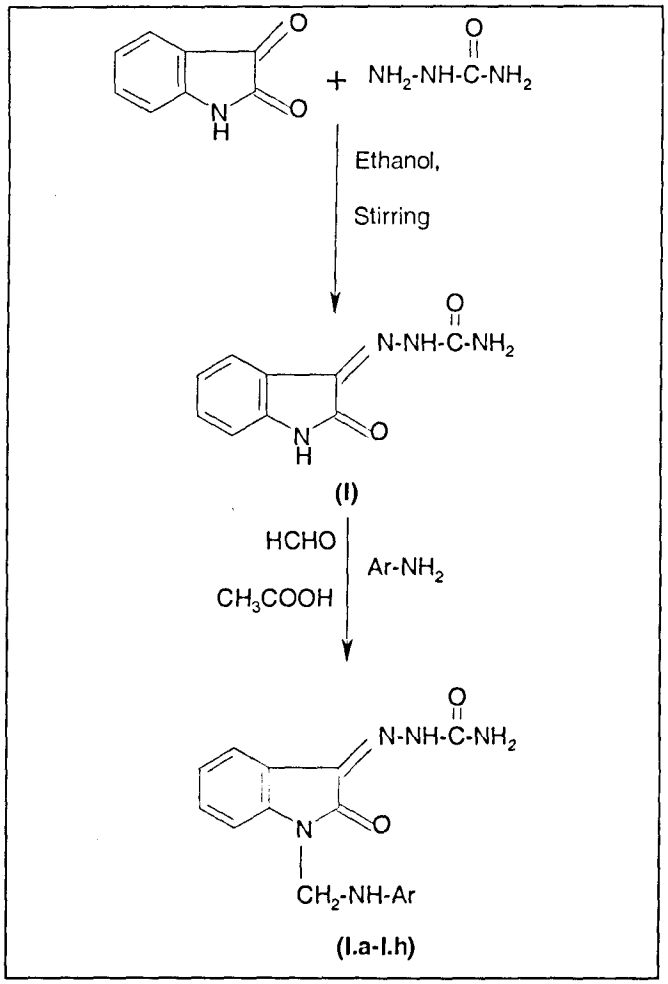
Isatin is an endogenous compound isolated in 1988[1] and reported to possess a wide range of central nervous system activities[2,3]. Isatin is the biologically active chemical produced by an *Alteromones* sp. strain inhabiting the surface of embryos of the cardiean shrimp *Palaemon macrodectylus*, which protects them from the pathogenic fungus *Lagenidium callinectus*[4]. Schiff bases and Mannich bases of Isatin were reported to possess antibacterial[5-7], antifungal[8-10], antiviral[11-16], antiprotozoal[17,18] and antihelmintic[19,20] 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°; 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, IH, 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. ($C_{18}H_{19}N_5O_3$) 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.

1-(4'-Chloroanilinomethyl)-3-semicarbazino isatin (Ib): IR (KBr) cm^{-1}: 3469, 3302, 3224 (N-H), 1710, 1695 (C=O), 1665 (C=N), 1590 (C=C); ^{1}H NMR ($CDCl_3$, DMSO-d_6)δ ppm:



Scheme 1: Synthesis of title compounds

2.499 (d 2H, -CH_2), 7.06 (t, 6H, Ar-H), 7.31 (t, 2H, Ar-H), 7.59 (t, 1H, -NH), 11.11 (s, 1H, -NH), 11.72 (s, 2H, -NH_2); Anal. ($C_{16}H_{14}N_5O_2Cl$) Found: C, 55.96%; H, 4.08%; N, 20.39%; Calculated: C, 55.97%; H, 4.08%; N, 20.40%

1-(4'-Bromoanilinomethyl)-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 ($CDCl_3$, DMSO-d_6) δ ppm: 2.487 (d, 2H, -CH_2), 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, -NH_2); Anal. ($C_{16}H_{14}N_5O_2Br$) Found: C, 49.48%; H, 3.59%; N, 18.04%; Calculated: C, 49.48%; H, 3.60%; N, 18.04%.

1-(4'-Fluoroanilinomethyl)-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 ($CDCl_3$, DMSO-d_6)δ ppm: 2.50 (d, 2H, -CH_2), 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, -NH_2); Anal. ($C_{16}H_{14}N_5O_2F$) Found: C, 58.71%; H, 4.27%; N, 21.40%; Calculated: C, 58.71%; H, 4.28%; N, 21.40%.

1-(4'-Aminopyridinylmethyl)-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 ($CDCl_3$, DMSO-d_6)δ ppm: 2.5 (d, 2H, -CH_2), 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, NH_2); Anal. ($C_{15}H_{14}N_6O_2$) 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 ($CDCl_3$, DMSO-d_6)δ ppm: 2.50 (d, 2H, -CH_2), 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, -NH_2); Anal. ($C_{16}H_{14}N_6O_4$) 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 ($CDCl_3$, DMSO-d_6)δ ppm: 2.50 (d, 2H, -CH_2), 3.68 (s, 3H, -OCH_3), 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, -NH_2); Anal. ($C_{17}H_{17}N_5O_3$) Found: C, 60.16%; H, 4.99%; N, 20.62%; Calculated: C, 60.17%; H, 5.01%; N, 20.64%.

1-(3'-Aminopyridinylmethyl)-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 ($CDCl_3$, DMSO-d_6)δ ppm: 2.49 (d, 2H, -CH_2), 7.16 (d, 5H, Ar-H), 7.41 (d, 2H, Ar-H),, 7.65 (d, 1H, N-CH), 7.82 (t, 1H, -NH), 10.96 (s, 1H, -NH), 11.70 (s, 2H, -NH_2); Anal. ($C_{15}H_{14}N_6O_2$) 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 an-

TABLE 1: PHYSICAL DATA OF 3-SEMICARBAZINO ISATIN DERIVATIVES

Compd. No.	Ar	Mol. Form.	R_f Value	mp (°)	Yield %
Ia	4'-ethoxyphenyl	$C_{18}H_{19}N_5O_3$	0.78	234	63
Ib	4'-chlorophenyl	$C_{16}H_{14}N_5O_2Cl$	0.61	242	79
Ic	4'-bromophenyl	$C_{15}H_{14}N_5O_2Br$	0.73	176	45
Id	4'-fluorophenyl	$C_{16}H_{14}N_5O_2F$	0.48	184	76
Ie	Pyridine-4'-yl	$C_{15}H_{14}N_6O_2$	0.60	238	37
If	4'-nitrophenyl	$C_{16}H_{14}N_6O_4$	0.65	252	79
Ig	3'-methoxyphenyl	$C_{17}H_{17}N_5O_3$	0.77	78	52
Ih	Pyridine-3'-yl	$C_{15}H_{14}N_6O_2$	0.55	170	49

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

TABLE 2: ANTIMICROBIAL ACTIVITY OF 3-SEMICARBAZINO ISATIN DERIVATIVES

Compd. No.	*E. coli*		*S. aureus*		*Candida albicans*	
	Zone of inhibition (mm)*	% activity compared to standard	Zone of inhibition (mm)*	% activity compared to standard	Zone of inhibition (mm)*	% activity compared to standard
Ia	21	91.30	20	76.92	21	87.50
Ib	19	82.60	16	61.53	18	75.00
Ic	19	82.60	21	80.76	19	79.16
Id	17	73.91	23	88.46	20	83.33
Ie	19	82.60	20	76.92	19	79.16
If	18	78.26	13	50.00	21	87.50
Ig	14	60.86	15	57.69	18	75.00
Ih	16	69.56	19	73.07	19	79.16
Amikacin	23	100.00	26	100.00	-	-
Fluconazole	-	-	-	-	24	100.00

Solvent used is dimethyl formamide (No zone of inhibition), *Average of three independent determinations, Sabouraude 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 Ia, Id, and Ie with *p*-ethoxyphenyl, *p*-fluorophenyl and pyridine-3'-yl group, respectively, exhibited most significant activity against *S. aureus* and *C. albicans*. Compound If having *p*-nitrophenyl group showed most significant activity against *C. albicans* but moderate activity against *S. aureus*. Compounds Ia, Ib, Ic and Ie with *p*-ethoxyphenyl, *p*-chlorophenyl, *p*-bromophenyl and pyridine-4'-yl group, respectively, exhibited very good activity against *E. coli* while compound Ig having 3'-methoxyphenyl group showed moderate activity against *E. coli*. Compound Ie with pyridine-4'-yl group exhibited better antimicrobial activity against *E. coli* as compared to compound Ih 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: Aristalochiasae) 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 bio-social and medicinal problems confronting mankind today[1]. 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[2], Kamboj and Dhawan[3] have exhaustively reviewed research on Indian plants with antifertility activity.

Aristalochia, 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 cleanings. The root of the plant is reported to contain aristalochic acid, which possesses tumor-inhibiting activity and has been used in the treatment of cancer, snakebite, and helmenthiasis[4].

It is reported that root extracts of *Aristalochia tagala* are used in female antifertility, as a tonic or emmenogogue and in the treatment of bowel complaints[5]. Literature survey revealed that no work was carried out on the leaves of

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