Synthesis of sulpha drug acridine derivatives and their evaluation for anti-inflammatory, analgesic and anticancer activity

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Various sulpha drugs i.e. sulphaacetamide, sulphathiazole, sulphadiazine and sulphamethazine were obtained from Aldrich or Sigma Chemical Company. 9-Chloro-2,4(4H) substituted acridines and 9-isothiocyanato-2, 4(4H) substituted acridines to give corresponding coupled products 3a-f and 4a-h respectively. The structures of all synthesized compounds have been confirmed by spectroscopic methods. Anti-inflammatory activity evaluation of 3a,b,e and 4a-h was carried out and compounds 4a, 4d, 4g and 4h showed 8, 13, 22 and 3% activity respectively at 100mg/kg p.o. Analgesic activity evaluation of 3a,b,e and 4a-h indicated that these compounds possess 25, 75, 50, 25, 50, 50, 0, 75, 50, 50 and 50% analgesic activity at 100mg/kg p.o. Anticancer activity evaluation of 3a-f and 4a-h against a small panel of seven cancer cell lines consisting of lung (NCI-H 460), colon (HT 29), melanoma (LOX); breast (MCF 7 and MCF 7 /ADR); prostate (DU I 45) and CNS (U251) tumors was carried out. Best GIs, concentration which inhibits the cell growth by 50% values are shown by 4b, 0.4 μM (lung carcinoma, cell line NCI-H 460); 4b, 0.3 μM (colon tumor, cell line HT 29); 3e, 7.2 μM (melanoma tumor, cell line LOX); 4b, 0.7 μM (breast tumor, cell line MCF7); 4c, 1.9 μM (breast tumor, cell line MCF7/ADR); 4b, 0.8 μM (prostate tumor, cell line DU 145) and 4b, 1.4 μM (CNS tumor, cell line U251) respectively. Out of all the compounds reported here GIs value shown by 4c i.e. 1.9 μM against breast tumor (MCF7/ADR) is quite close to the GIs value i.e. 1.2 μM of the standard drug doxorubicin. Also it is worthwhile to mention here that compound 4b, has shown good anticancer activity against four tumor cell lines i.e. GIs value < 1 μM.

The major problems faced by mankind are cancer and inflammatory diseases. A number of anti-inflammatory drugs available in market have serious side effects1 and hence cannot be used continuously for long time. Only a few anticancer drugs are available in the market and hence there is an urgent need to develop new safer anti-inflammatory remedies2,3,4 and search for new anticancer agents5,6. Acridine derivatives possessing anti-inflammatory & analgesic7,8 and anticancer9-11 activities have been reported in literature.

In continuation of our efforts in search of potential anti-inflammatory14-22 and anticancer agents24-28 we have synthesized a variety of sulphadrug acridine derivatives and screened them for anti-inflammatory, analgesic and anticancer activities which we wish to report in this paper.

Sulphaacetamide, sulphathiazole, sulphadiazine and sulphamethazine were obtained from Aldrich or Sigma Chemical Company. 9-Chloro-2,4(4H) substituted acridines were synthesized by following reaction procedure reported in literature29,30. Equimolar quantities of 9-chloro-2,4(4H) substituted acridines 1 and sulphadugs were dissolved separately in minimum amount of methanol and then both the solutions were mixed. The reaction contents were allowed to stand at room temperature for one to ten days and then solvent was removed under reduced pressure and the residue was treated with 10% aq. sodium carbonate solution to give crude condensed product, which was purified by crystallization or column chromatography to give pure compounds 3a-f (Scheme 1). Structures assigned to compounds 3a-f are supported by correct IR, 1HNMR and HRES or HRMS spectral data reported in Table 1.
9-isothiocyanato-2,4-(un)substituted acridines 2 were prepared by following reaction procedure reported in literature. Condensation of various sulphadruugs with 2 was carried out at room temperature using THF or DMF as solvent of reaction to give condensed products 4a-h (Scheme I). These products were purified by column chromatography or by crystallization to give pure products 4a-h. The structures assigned to 4a-h are supported by correct IR, $^1$H NMR and HRES or HRMS spectral data reported in Table I.
Table I—Physical constants and spectral data of sulfa drug acridine derivatives 3a-f and 4a-h

<table>
<thead>
<tr>
<th>Compd</th>
<th>Solvent or cryst. fusion</th>
<th>m.p. °C</th>
<th>Yield %</th>
<th>IR (KBr) νmax in cm⁻¹</th>
<th>¹H NMR (DMSO-d₆, δ, J (Hz))</th>
<th>HRMS or HRES or LRES m/z (%)</th>
</tr>
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<tbody>
<tr>
<td>3a</td>
<td>MeOH</td>
<td>205</td>
<td>89</td>
<td>3407 (-NH-), 1579 (- CO NH-), 1515 (Ar), 1254 &amp; 1133 (-NHSO₂⁻)</td>
<td>1.93 (s, 3H, CH₃), 6.90 (m, 3H, Ar), 7.70 (m, 9H, Ar)</td>
<td>Found: 392.10616 (MH⁺, 100). Caled for C₁₉H₁₈N₂O₈S 392.10634.</td>
</tr>
<tr>
<td>3b</td>
<td>CHCl₃:EA (5:5)</td>
<td>170</td>
<td>40</td>
<td>3401 &amp; 3220 (-NH-), 1583 (-CONH-), 1509 (Ar)</td>
<td>1.80 (s, 3H, CH₃), 2.30 (s, 3H, CH₃), 6.60 (d, 1H, Ar), 6.80 (d, 1H, Ar), 7.70 (m, 3H, Ar), 7.70 (m, 8H, Ar)</td>
<td>Found: 406.122787 (MH⁺, 100%). Caled for C₁₉H₁₈N₂O₈S: 406.12259.</td>
</tr>
<tr>
<td>3c</td>
<td>Benzene:EA (5:5)</td>
<td>230</td>
<td>23</td>
<td>3380 &amp; 3304 (-NH-), 1521 (Ar), 1275 &amp; 1133 (-NHSO₂⁻)</td>
<td>(DMSO-d₆, +D₂O) δ 3.7 (s, 3H, δCH₃), 7.0 (d, 1H, Ar), 7.50 (d, 2H, Ar), 7.70-8.50 (m, 9H, Ar), 8.60 (d, 1H, Ar)</td>
<td>Did not give M⁺ ion peak but gave peaks at 209.08390.</td>
</tr>
<tr>
<td>3d</td>
<td>Benzene: EA (6:4) (d)</td>
<td>252</td>
<td>41</td>
<td>3430 (-NH-), 1583 &amp; 1503 (Ar), 1263 &amp; 1156 (-NHSO₂⁻)</td>
<td>(DMSO-d₆, +D₂O) δ 3.5 (s, 3H, OCH₃), 7.1 (t, 1H, Ar), 7.3 (s, 1H, Ar), 7.40 (d, 2H, Ar), 7.60 (m, 1H, Ar), 7.80 (dd, 1H, Ar), 8.0 (m, 3H, Ar), 8.1 (m, 3H, Ar), 8.5 (d, 2H, Ar)</td>
<td>Found: 457.12184 (M⁺, 100.00). Caled for C₁₉H₁₈N₂O₈S 457.12187.</td>
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<tr>
<td>3e</td>
<td>CCl₄:EA (2:8)</td>
<td>230</td>
<td>90</td>
<td>3454 &amp; 3377 (-NH-), 1593 &amp; 1500 (Ar), 1269 &amp; 1147 (-NHSO₂⁻)</td>
<td>2.3 (s, 3H, CH₃), 7.2 (t, 2H, Ar), 7.5 (m, 4H, Ar), 7.7 (t, 2H, Ar), 8.1-8.30 (m, 6H, Ar), 11.60 (bs, 1H, -NH-), 11.85 (s, 1H, -NH-.)</td>
<td>Found: 442.13341 (MH⁺, 100%). Caled for C₁₉H₁₈N₂O₈S: 442.13322.</td>
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<tr>
<td>3f</td>
<td>MeOH</td>
<td>240</td>
<td>88</td>
<td>3429 (-NH-), 1579 &amp; 1504 (Ar), 1276 &amp; 1156 (-NHSO₂⁻)</td>
<td>2.30-2.32 (two singlets looking like a doublet 6H, 2 x CH₃), 6.87-6.95 (d, 1H, Ar), 7.41-7.48 (d, 3H, Ar), 7.89-8.20 (m, 8H, Ar), 8.33-8.35 (d, 1H, Ar), 11.40 (bs, 2H, -NH-.)</td>
<td>Found: 456.14939 (MH⁺, 100%). Caled for C₁₉H₁₈N₂O₈S: 456.14887.</td>
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<tr>
<td>4a</td>
<td>MeOH</td>
<td>215</td>
<td>45</td>
<td>3438 (-NH-), 1519 &amp; 1414 (Ar), 1273 &amp; 1141 (-NHSO₂⁻)</td>
<td>δ 3.60 (s, 3H, OCH₃), 6.80 (d, 1H, Ar), 7.20-7.50 (m, 6H, Ar), 7.70 (m, 2H, Ar), 8.00 (t, 1H, Ar), 8.20 (m, 3H, Ar)</td>
<td>HRES show (MH⁺ - HSCN, 100%) peak at 463.09827.</td>
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<table>
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<tr>
<th>Compd</th>
<th>Solvent of crystallization</th>
<th>m.p. °C</th>
<th>Yield %</th>
<th>IR (KBr) νmax in cm⁻¹</th>
<th>¹H NMR (DMSO-d₆) δ, J (Hz)</th>
<th>HRMS or HRES or LRES m/z (%)</th>
</tr>
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<tbody>
<tr>
<td>4b</td>
<td>CHCl₃:EA (8:2)</td>
<td>&gt;230</td>
<td>11</td>
<td>3422 &amp; 3358 (-NH-), 1645 (C=N), 1585 &amp; 1493 (Ar), 1324 &amp; 1153 (-NHSO₂⁻)</td>
<td>6.00 (d, 3H, Ar), 6.50 (d, 3H, Ar), 7.00 (t, 2H, Ar), 7.60 (d, 4H, Ar), 8.50 (d, 3H, Ar)</td>
<td>252.1 ( ), 5.0% , 218</td>
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<tr>
<td>4c</td>
<td>CHCl₃:Pet. ether (5:5)</td>
<td>&gt;220</td>
<td>17</td>
<td>3467 &amp; 3250 (-NH-), 15 65 (Ar), 1227 &amp; 1162 (-NHSO₂⁻)</td>
<td>2.47 (s, 3H, -CH₃), 7.2 (t, 2H, Ar), 7.42-7.75 (m, 10H, Ar), 8.0 (s, 1H, Ar), 8.25 (d, 1H, Ar), 11.67 (bs, 2H, 2 x NH), 12.7 (s, 1H, NH)</td>
<td>225.06116 ( ), 60.53%</td>
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<tr>
<td>4d</td>
<td>MeOH</td>
<td>225</td>
<td>85</td>
<td>3403 (-NH-), 1581 (C=N), 1503 &amp; 1429 (Ar), 1262 &amp; 1155 (-NHSO₂⁻)</td>
<td>3.50 (s, 3H, OCH₃), 6.78 (bs, 1H, -NH-), 7.10 (t, 1H, Ar), 7.20-7.40 (m, 4H, Ar), 7.80 (d, 1H, Ar), 8.00-8.20 (m, 6H, Ar), 8.50 (d, 2H, Ar)</td>
<td>224.05299 ( ), 41.19%</td>
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<tr>
<td>4e</td>
<td>Pet. ether: CHCl₃ (8:2)</td>
<td>220</td>
<td>16</td>
<td>3490 &amp; 3400 (-NH-), 15 69 (Ar), 1223 &amp; 1160 (-NHSO₂⁻)</td>
<td>2.60 (s, 3H, CH₃), 7.30 (m, 4H, Ar), 7.80 (m, 5H, Ar), 8.20 (d, 2H, Ar), 8.80 (dd, 3H, Ar), 10.60 (s, 1H, -NH-), 11.40 (s, 2H, 2 x –NH-)</td>
<td>225.06117 ( ), 90.12%</td>
</tr>
</tbody>
</table>

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Anti-inflammatory activity evaluation of compounds 3a, b, e and 4a-h was carried out at 100 mg/kg p.o. in rats using carrageenin induced paw oedema. Compounds 4a, 4d, 4g and 4h showed 8,13,22 and 3% activity respectively whereas others showed no effect. Analgesic activity of compounds 3a, b, e and 4a-h was evaluated by the writhing assay. Compounds 3a, b, e and 4a-h exhibited 25, 75, 50, 25, 50, 0, 75, 50, 50 and 50% analgesic activity at 100 mg/kg p.o. respectively. Compounds 3b, e and 4b, c, e, g, h displayed 50, 25, 25, 25 and 25% activity at 50 mg/kg p.o respectively.

Anticancer activity evaluation of 3a-f and 4a-h was carried out against a small panel of seven cancer cell lines consisting lung (NCH460); colon (HT29); melanoma (LOX); breast (MCF7, MCF7/ADR); prostate (DU145) and CNS (U251) tumors. The effect of the compounds screened is expressed in terms of 50% growth inhibition concentration (GI50). The GI50 values (μM concentration) of 3a-f and 4a-h are reported in Table II. From Table II it is clear that best GI50 values are shown by 4c i.e. 1.9 μM against breast tumor (MCF7/ADR) is quite close to the GI50 value i.e. 1.2 μM of the standard drug doxorubicin. Also it is worthwhile to mention here that compound 4b, has shown good anticancer activity against four tumor cell lines i.e. GI50 value < 1 μM.

**Experimental Section**

Melting points were determined on JSGW apparatus and are uncorrected. Only principal sharply defined IR peaks are reported. 1H NMR spectra were recorded in ca 5-15% (w/v) solution in DMSO-d6 using a Varian XL-300 spectrometer. Line positions are recorded in ppm from the reference. The MS spectrometer peak measurements were made by comparison with perfluorotributylamine using AEI MS-9 double focusing high-resolution mass spectrometer at a resolving power of 15,000. TLC was performed on silica gel G. for TLC (Merck) and spots were visualized by iodine vapour or by irradiation with UV light (254nm). Column chromatography was performed by using Qilgins silica gel for column chromatography (60-120 mesh).

**General procedure for 3**

Condensation of 9-chloroacridine with sulfacetamide 3a. Sulfacetamide (400 mg; 1.86 mmole) and 9-chloroacridine (400 mg; 1.87 mmole) were dissolved separately in methanol (25 mL for each) by

<table>
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<tr>
<th>Compd</th>
<th>Solvent of cryst/elution</th>
<th>m.p. °C</th>
<th>Yield %</th>
<th>IR (KBr) νmax in cm⁻¹</th>
<th>¹H NMR (DMSO-d6) δ, J (Hz)</th>
<th>HRMS or HRES or LRES m/z (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4f</td>
<td>MeOH</td>
<td>198</td>
<td>47</td>
<td>3445 &amp; 3389 (NH-), 1583 (C=O), 1502 &amp; 1424 (Ar), 1274 &amp; 1155 (NHSO₂⁻)</td>
<td>2.27-2.30 (2s, looking like a doublet, 6H, 2x CH₃), 6.90 (d, 1H, Ar), 7.30 (d, 3H, Ar), 7.90-8.10 (m 8H, Ar)</td>
<td>456.0 (MH⁺ - HSCN, 100%).</td>
</tr>
<tr>
<td>4g</td>
<td>MeOH</td>
<td>&gt;230</td>
<td>68</td>
<td>3404 (NH-), 1583 (C=O), 1504 &amp; 1410 (Ar), 1278 &amp; 1155 (NHSO₂⁻)</td>
<td>2.30 (s, 3H, -CH₃), 3.53 (s, 3H, OCH₃), 6.95 (d, 1H, Ar), 7.38-7.72 (m, 6H, 5H Ar + NH), 7.95 (d, 3H, Ar), 8.16 (m, 3H, Ar), 8.32 (d, 1H, Ar)</td>
<td>472.1 (MH⁺ - HSCN, 100%).</td>
</tr>
<tr>
<td>4h</td>
<td>MeOH</td>
<td>&gt;230</td>
<td>35</td>
<td>3405 (NH-), 1654 (C=N), 1505 (Ar), 1265 &amp; 1115 (NHSO₂⁻)</td>
<td>2.70 (s, 6H, 2x CH₃), 7.35 (t, 2H, Ar), 7.46 (t, 2H, Ar), 7.70 (d, 2H, Ar), 7.83 (t, 2H, Ar), 8.06 (d, 2H, Ar), 8.15 (d, 2H, Ar), 8.50 (d, 2H, Ar)</td>
<td>209.1 (100%).</td>
</tr>
</tbody>
</table>
Condensation of sulfaacetamide with 9-chloro-2-methylacridine 3b. Sulphaacetamide (400 mg; 1.86 mmole) and 9-chloro-2-methylacridine (425 mg; 1.86 mmole) were dissolved separately in methanol (40 and 50 mL respectively) by warming. Both the solutions were cooled at room temperature and then mixed together and allowed to stand at room temperature for nine days. Solvent was removed under reduced pressure and the solid residue left behind was suspended in 10% sodium carbonate solution (20 mL) and stirred for 30 min. It was then filtered, washed with water and air dried to give crude product 3a. Compound 3a was recrystallized from methanol to give pure condensed product 3a. Yield, m.p. and spectral data of 3a is reported in Table I.

Condensation of sulfaacetamide with 9-chloro-2-methylacridine 3b. Sulphaacetamide (400 mg; 1.86 mmole) and 9-chloro-2-methylacridine (425 mg; 1.86 mmole) were dissolved separately in methanol (40 and 50 mL respectively) by warming. Both the solutions were cooled at room temperature and then mixed together and allowed to stand at room temperature for nine days. Solvent was removed under reduced pressure and the solid residue left behind was suspended in 10% sodium carbonate solution (20 mL) and stirred for 30 min. It was then filtered, washed with water and air dried to give crude product 3a. Compound 3a was recrystallized from methanol to give pure condensed product 3a. Yield, m.p. and spectral data of 3a is reported in Table I.

Condensation of 9-chloro-2-methylacridine with sulfamerazine 3f. Sulphamerazine (265 mg; 1 mmole) and 9-chloro-2-methylacridine (230 mg; 1.01 mmole) were dissolved separately in methanol (30 and 20 mL respectively). These solutions were mixed together and then allowed to stand at room temperature for one day. Solid product separated out was filtered and washed with chilled methanol to give condensed product 3f. Solvent from the filtrate was removed under reduced pressure and the residue left behind was washed with chilled methanol to give second crop of 3f. Combined amount of 3f was stirred with 10% aq. sodium carbonate (20 mL) for half an hr. and then filtered washed with water and air dried to give crude 3f which was crystallized from methanol to give pure 3f. Yield, m.p. and spectral data of 3f is reported in Table I.

General procedure for 4
Condensation of 9-isothiocyanato-2-methoxyacridine with sulfathiazole 4a. Sulphathiazole (255 mg, 1 mmole) and 9-isothiocyanato-2-methoxyacridine (266 mg, 1 mmole) were dissolved separately in DMF (5 and 10 mL respectively) and then mixed together. Reaction contents were allowed to stand at room temperature for two days. DMF was removed completely using high vacuum. To the solid residue left behind was added methanol (10 mL). Solid product separated out was filtered, washed with CHCl₃ (~5 mL) and then with ether to give 4a. Crude 4a was further purified by crystallization from methanol to give pure 4a.
Similarly were prepared 4g and 4h. Yield, m.p.
solvent of crystallization and spectral data of 4a, 4g
and 4h are reported in Table I.

Condensation of sulphadiazine with 9-isothiocyanatoacridine 4b. Sulphadiazine (250 mg;
1 mmole) and 9-isothiocyanatoacridine (240 mg;
1 mmole) were dissolved separately in THF (50 and
100 mL respectively). Two solutions were mixed to­
gether and heated under reflux for 8 hr and then sol­
vent was removed under reduced pressure. Solid resi­
due so obtained was subjected to column chromato­
graphy over silica gel. Solvent of elution, yield, m.p.
and spectral data of 4b are reported in Table I.

Condensation of sulphadiazine with 9-isothio­
cyanato-2-methylacridine 4c. Sulphadiazine (250 mg;
1 mmole) and 9-isothiocyanato-2-methylacridine
(250 mg, 1 mmole) were dissolved separately in THF
(40 and 100 mL respectively). Both the solutions
were mixed together and allowed to stand at room tem­
perature for 3 days. Solvent was removed under reduced
pressure and the solid residue so obtained was sub­
jected to column chromatography over silica gel. Sol­
vent of elution, yield, m.p and spectral data of 4c are
reported in Table I.

Similarly were prepared 4e and 4f. Physical con­
stants and spectral data of 4e and 4f are reported in
Table I.

Condensation of sulphadiazine with 9-
isothiocyanato-2-methoxyacridine 4d. Sulfadiazine
(250 mg; 1 mmole) and 9-isothiocyanato-2-methoxyacri­
dine (266 mg, 1 mmole) were dissolved separately in
DMF (5 and 10 mL respectively). Both the solu­
tions were mixed together and allowed to stand at room
temperature for two days. DMF was removed com­
pletely under high vacuum and solid residue was sub­
jected to column chromatography over silica gel. Sol­
vant of elution, yield, m.p and spectral data of 4d are
reported in Table I.

Anti-inflammatory activity screening. Anti-inflam­
matorv activity screening was carried out using carragee­
in-induced paw oedema in albino rats obtained from the animal facility of the Central Drug
Research Institute, Lucknow and maintained under
standard laboratory conditions. The oedema in one of
the hind paws was induced by injection of carragee­
in (100mm³ of 1%) into planter apponeurosis. The vol­
ume of the paw was measured plethysmographically
immediately after and three hours after the injection
of the irritant. The difference in volume gave the
amount of oedema developed. Percent inhibition of
the oedema between the control group and compound
treated groups was calculated and compared with the
group receiving a standard drug. At 100 mg/kg p.o
compounds 4a, 4d, 4g and 4h inhibited carragee­
in induced hind paw oedema by 8, 13, 22 and 3% re­
spectively, as compared to the standard drug ibupro­
fen which showed 51% activity at 50 mg/kg p.o.

Analgesic activity evaluation. Analgesia was mea­
sured by the writhing assay using Swiss mice
(15-20 g) bred in the animal house of the Central
Drug Research Institute, Lucknow and maintained
under standard laboratory conditions. Female mice
were screened for writhing on day 1 by injecting
intraperitoneally 0.2 cm³ of aq. solution of phenyl­
quinone. They were kept on flat surface and the num­
ber of writhes of each mouse was recorded for 20
min. The mice showing significant writhes (>10) were
sorted out and used for analgesic assay on the follow­
ing day. The mice consisting of 5 in each group and
showing significant writhing were given orally a 50 or
100 mg/kg p.o dose of the test compounds 15min.
prior to phenylquinone challenge. Writhing was again
recorded for each mouse in a group and a percentage
protection was calculated using formula.

Protection=100-{[(no. of writhings for treated
mice)/ (no. of writhings for untreated mice)] ×100}.

This was taken percent analgesia response and was
averaged in each group of mice. Percent of animals
exhibiting analgesia was determined with each dose.
Compounds 3a,b,e and 4a-h were screened for anal­
gesic activity. Compounds 3a,b,e and 4a-h exhibited
25,75,50,25,50,50,0,75,50,50 and 50% analgesic ac­

ivity at 100 mg/kg p.o. Compounds 3b,e and
4b,c,e,g,h displayed 50,25,25,25,50,25 and 25% ac­

ivity at 50 mg/kg p.o. respectively.

Anticancer activity screening. Compounds 3a-f
and 4a-h were tested over a broad concentration range
(ten fold dilutions starting from >100 µM to 10 nM)
against seven human cancer cell lines comprised of
different tumor types maintained in growing condition
in RPMI 1640 medium containing 10% fetal calf se­
rum and incubated at 37°C under 5% CO₂ atmos­
phere. All cell lines were inoculated on to series of
standard 96 well microtitre plate on day zero followed
by 24 hr incubation in the absence of test compound.
The inoculation density used currently in the screen
was as per Monk et al. All the test compounds i.e.
3a-f and 4a-h were dissolved in DMSO and diluted
further in culture medium. An aliquot of each dilution
was added to the growing cells 96well plates and incu­
bated for 48hr. After incubation, the assay was ter­
minalized by adding 50 µL of trichloroacetic acid
(TCA) and incubating at 4°C for 30 min. The precipitated cells were washed and stained with sulforhodamine B dye for 30 min and the excess dye was washed off with acetic acid. Absorbed dye is solubilized in trisbase (alkaline pH) and quantitated by measuring the OD at 490 nm in an ELISA reader. GI50 values were calculated according to Boyd and Paul18 and are reported in Table II.

Acknowledgement

We are grateful to Head of RSIC Lucknow, Prof J W Lown, Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada and technical staff of the Chemistry Department, University of Roorkee for spectroscopic studies. Our sincere thanks go to the director of CDRI Lucknow for providing testing facilities and to Ms U Sharma and Mr H C Verma for technical help in conducting anti-inflammatory and analgesic activity tests respectively. Financial help from UGC, New Delhi (Monika Johar) is gratefully acknowledged.

References
