

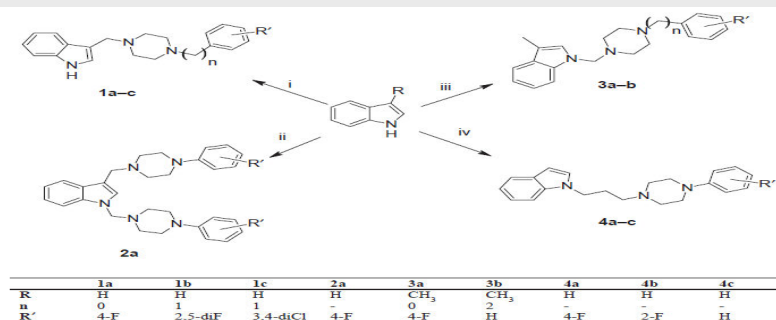
## Synthesis and anticancer screening studies of indole-based piperazine derivatives

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### Abstract

The preparation of the compounds is illustrated in Scheme 1. The groups of 3-{[4-(substitutedphenyl / benzyl)piperazin-1-yl]methyl}-1H-indole 1a-c, 1,3-di-{[4-(4-fluorophenyl)piperazin-1-yl]methyl}-1H-indole 2a and 1-{[4-(substitutedphenyl / phenylethyl)piperazin-1-yl]methyl}-3-methyl-1H-indole 3a-b were prepared by Mannich reaction of substituted piperazine and formaldehyde with indole or 3-methylindole. The crude products were purified by recrystallization or column chromatography. 1-{3-[4-(substitutedphenyl)piperazin-1-yl]propyl}-1H-indole 4a-c were synthesized by the reaction of indole and 1-(3-chloropropyl)-4-(substitutedphenyl)piperazine in presence of potassium hydroxide. To obtain 1-(3-chloropropyl)-4-(substitutedphenyl)piperazine, substituted phenyl piperazine was reacted with 1-bromo-3-chloropropane. Compounds 4a-c were purified by column chromatography on silica gel using ethyl acetate / n-hexane as a mobile phase system (Scheme 1). Structures of compounds were clarified with IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, mass spectroscopies and elemental analyses.



**Scheme 1:** Synthesis of compounds 1a-c, 2a, 3a-b, and 4a-c. Reagent and conditions: (i) HCHO, substituted piperazine, EtOH, room temperature; (ii) HCHO, 4-F-phenylpiperazine, EtOH, reflux, 4 h; (iii) HCHO, substituted piperazine, EtOH, reflux, 4 h; and (iv) 87% KOH, DMSO, room temperature, 1 h; 1-(3-chloropropyl)-4-(substitutedphenyl)piperazine, DMSO, 0 °C, 20h.

The cytotoxic activity of the synthesized compounds was investigated on liver (HUH7), breast (MCF7), and colon (HCT116) cancer cell lines, by means of sulphorhodamine B (SRB) assays in triplicate. Among compounds, the best inhibitory activity against HUH7 (IC<sub>50</sub>=3.42 μM) was exhibited by compound 1c (3-{[4-(3,4-dichlorobenzyl)piperazin-1-yl]methyl}-1H-indole).

### Biography:

Professor Yarim has studied anticancer drug design for 20+ years, during which time she has authored several peer-reviewed reports. She has served on numerous review committees for the National Science Foundation in Turkey.