Biological Activity of 1-Aryl-3-phenethylamino-1-propanone Hydrochlorides and 3-Aroyl-4-aryl-1-phenethyl-4-piperidinols on PC-3 Cells and DNA Topoisomerase I Enzyme

Ebru Mete, Halise Inci Gul*, Pakize Canturk, Zeki Topcu, Bulbul Pandit, Mustafa Gul, and Pui-Kai Li

a Department of Chemistry, Faculty of Sciences, Ataturk University, 25240, Erzurum, Turkey
b Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Ataturk University, 25240, Erzurum, Turkey. Fax: 90-442-2360962. E-mail: incigul1967@yahoo.com
c Department of Pharmaceutical Biotechnology, Faculty of Pharmacy, Ege University, Izmir, Turkey
d Division of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, The Ohio State University, Columbus, OH 43210, USA
e Department of Physiology, Faculty of Medicine, Ataturk University, 25240, Erzurum, Turkey

* Author for correspondence and reprint requests

A number of studies reported Mannich bases to manifest antimicrobial, cytotoxic, anticancer, anti-inflammatory, and anticonvulsant activities. A considerable number of therapeutically important cytotoxic compounds are active on DNA topoisomerases that regulate the DNA topology. In the present study we evaluated the biological activity of mono-Mannich bases, 1-aryl-3-phenethylamino-1-propanone hydrochlorides (1a–10a), and semicyclic mono-Mannich bases, 3-aroyl-4-aryl-1-phenethyl-4-piperidinols (1b–9b), synthesized in our laboratory. We employed androgen-independent human prostate cancer cells (PC-3) to assess the cytotoxicity of the compounds and extended the biological activity evaluation to cover supercoil relaxation assays of mammalian type I topoisomerases. Our results showed that the compounds had cytotoxicity within the 8.2–32.1 µM range, while two compounds gave rise to a comparable average value in topo I interference of 42% and 40% for 10a (with a hydroxy substituent on the phenyl ring from mono-Mannich bases) and 5b (with a fluoro substituent on the phenyl ring from the semicyclic mono-Mannich base series, piperidinols), respectively.

Key words: Mono-Mannich Bases, Cytotoxic Activity, PC-3 Cell, DNA Topoisomerase I