Synthesis and cytotoxicity evaluation of *N*-(2-oxo-2-((5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl)amino)ethyl)-2-phenylacetamide derivatives as apoptosis inducers with potential anticancer effects

Farzad Ramezani [a*], Alireza Aliabadi [b], Ahmad Mohammadi Farani [c]

Authors' Affiliations:
[a] Students Research Committee, Faculty of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran;
[b] Department of Medicinal Chemistry, Faculty of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran;
[c] Department of Pharmacology and Toxicology, Faculty of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran;

Abstract Presenter:
Farzad Ramezani; PharmD; Students Research Committee, Faculty of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, MI 3750475989, Iran;
E-mail: ramezani9858@gmail.com
Mailingaddress: Faculty of Pharmacy School, Daneshgah Street, Kermanshah, Iran;

****Correspondence:***
Farzad Ramezani; PharmD; Students Research Committee, Faculty of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, MI 3750475989, Iran;
E-mail: ramezani9858@gmail.com
Mailingaddress: Faculty of Pharmacy School, Daneshgah Street, Kermanshah, Iran;

Abstract

Introduction: The statistics show that the numbers of cancer reports is increasing and need for development of new anticancer drugs is a principal aim in current medicinal chemistry. Due to very limitations of current antineoplastic therapeutics such as high incidence of adverse effects and intuitive resistance of tumor, discovery of new anticancer agents feel to be crucial.

Methods and Results: Synthesis and cytotoxicity assessment of 1,3,4-thiadiazole derivatives led to the discovery of new compounds with potential anticancer activity. MTT assay was done against three cancerous cell lines containing PC3 (prostate carcinoma), HT-29 (human colon adenocarcinoma) and SKNMC(neuroblastoma) in comparison with doxorubicin as reference drug. All synthesized compounds were identified using spectroscopic techniques like ^{1}HNMR, IR and MS. The synthesized derivatives were afforded with high yields. All target compounds were tested against MCF-7 (breast cancer), H1299 (non-small cell lung carcinoma), A2780 (ovarian carcinoma). Tested derivatives exhibited favorable anticancer activity *in vitro* compared to doxorubicin in MTT assay. Various derivatives such as Cl, Br, CH_3 and F substituents were the best moieties for *para* positions of the phenyl ring (less than 1 µM). Some of tested compounds with these moieties showed superior activity than doxorubicin. Caspases activation was also explored for tested derivatives.

Conclusions: The 1,3,4-thiadiazole derivatives that prepared in the current project displayed significant anticancer activity and apoptosis induction. These agents could be proposed as novel anticancer lead compounds.

Key words: Synthesis; 1,3,4-Thiadiazole, Cytotoxicity, Anticancer