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to plasma protein (%unbound) based on the structure of the molecules. Finally, the percent of the drug bound to plasma proteins (PPB) was calculated by PreAdmet software (https://preadmet.bmdrc.kr/adme/) for all compounds observed.

RESULTS:

Retention constants, R_M^0 for 13 newly synthesized 1-aryl-3-methyl succinimide derivates obtained by using thin-layerv reversed-phase chromatography were applied as measurement of anisotropic lipophilicity. The values of the volume of distribution and plasma protein binding affinity varied depending on the software applied, but regardless of the applied software small distribution volumes and high protein binding affinity are expected for these compounds. Nevertheless, statistically significant parabolic correlation (r^2=0.968, $p<0.001$) was described between volume of distribution (i-lab 2.0 software) and anisotropic lipophilicity followed by statistically significant parabolic association (r^2=0.965, $p<0.001$) between volume of distribution in stationary state, Vdss, (pkCSM software) and experimentally determined anisotropic lipophilicity, RM0 for the analyzed compounds. Furthermore, the fraction of the drug unbound to plasma proteins (calculated with pkCSM software) was correlated with anisotropic lipophilicity of the analyzed compounds and parabolic association was obtained with high statistical quality (r^2=0.497, $p=0.013$). In addition, the percent of the drug bound to plasma proteins, PPB (PreAdmet software) was associated with anisotropic lipophilicity for observed series of succinimide derivatives with statistical significance (r^2=0.799, $p<0.001$).

CONCLUSIONS:

Lipophilicity is the primary underlying structural property that governs the distribution of 1-aryl-3-methyl succinimide derivates and their affinity to bind to plasma proteins. Introducing more lipophilic substituent in the 1-aryl-3-methyl succinimide core consequently results with increased volume of distribution followed by enhanced plasma protein affinity. One should be careful when making structural modifications that change lipophilicity in order to adjust an ADMET property since other properties that are affected by lipophilicity may be altered as well and should be monitored.

T3-P-13 Acrylamide treatment affects oxidative stress parameters in rat hepatocytes

Jelena Marković Filipović[51], Danijela Kojić[51], Marko Miler[51], Verica Milošević[52], Milica Matavulj[52]

KEYWORDS: acrylamide; hepatocytes; nitrite; gluthatione; lipid peroxidation

INTRODUCTION:

Acrylamide (AA) is industrial toxic substance with neurotoxic and reprotoxic effects. AA is a Maillard reaction product formed during processing of starchy food at high temperature.

OBJECTIVES:

The objective of our study was to determine whether acrylamide treatment disturbs redox balance by altering nitrite, glutathione (GSH), and malondialdehyde levels in rat hepatoma cell line (H4IIE).

METHOD / DESIGN:

Rat hepatoma cell line H4IIE was treated with 4 mM (IC_{20}) and 4.5 mM (IC_{50}) of AA for 24 h. The nitrite level in the medium was

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analyzed as an indicator of NO production following the Griess reaction method. After ultrasonic cell lysis in 2.5% sulfocalicylic acid, supernatant was analysed for the content of gluthatione. Lipid peroxidation was evaluated using thiobarbituric acid reactive substance assay (TBARS).

RESULTS:

Detected nitrite, malondialdehyde and GSH levels in rat hepatoma cell line H4IIE after acrylamide treatment are shown in *Figure 1*.

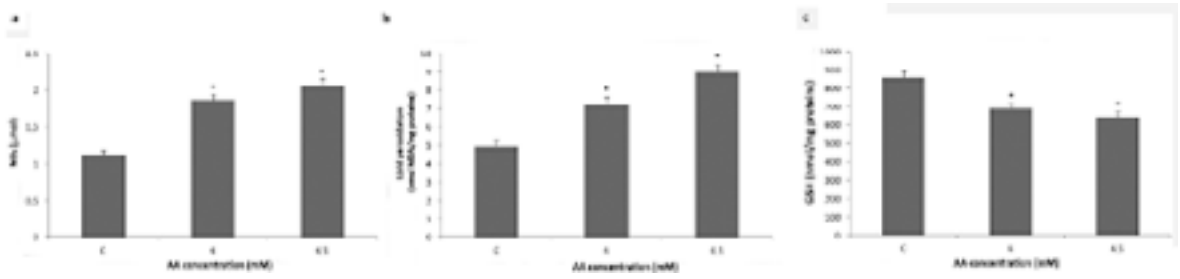

*Figure 1. Nitrite concentration (a), malondialdehyde (MDA) concentration (b), reduced glutathione (GSH) concentration (c) in H4IIE cells after treatment with 4 and 4.5 mM acrylamide (AA) for 24 h. Values in charts are means ± SEM of three experiments performed in triplicate. Mean values were significantly different from that of untreated control cells (*p<0.05).*

CONCLUSIONS:

In rat hepatoma cell line H4IIE, exposure to AA caused significant concentration-dependent increase of nitrite level and lipid peroxidation (*Fig. 1a, b*). On the other hand, GSH content significantly decreased in a concentration-dependent manner in H4IIE cells (*Fig.1c*). Obtained results indicate that AA disturbs redox status in hepatocytes.

T3-P-14 Multi-targeted anticancer activity of human amniotic membrane homogenate on various cancer cells

Aleksandar Janev[53], Taja Železnik Ramuta[53], Larisa Tratnjek[53], Žiga Sardoč[53], Hristina Obradović[54], Slavko Mojsilović[54], Milena Taskovska[55/56], Tomaž Smrkolj[55/56] and Mateja Erdani Kreft[53]

KEYWORDS: bladder cancer; human amniotic membrane; anticancer activity, 2D and 3D in vitro models

INTRODUCTION:

Based on the 2020 GLOBOCAN data, bladder cancer ranks as one of the ten most common cancer types throughout the world. Despite its increasing incidence and high recurrence rates, there have been no significant improvements in the standard treatment options of bladder cancer. Human amniotic membrane (hAM) is an innermost fetal membrane, which is associated with a wide range of biological properties such as anti-inflammatory, anti-fibrotic and anti-microbial activity. Furthermore, recent studies have underlined the possibility that human amniotic membrane (hAM) might also act as a promising anti-cancer agent.

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