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CYTOPROTECTIVE IMPACT OF CHRYSIN (5, 7- DIHYDROXYFLAVONE) UPON CYCLOPHOSPHAMIDE-ADMINISTERED EXPERIMENTAL ANIMALS

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Chemotherapeutics are widely recognized for their adverse side-effects during anti-cancer regiments. One of the complementary approaches to circumvent this dilemma could be the exploitation of natural compounds, which could optimally counteract the cellular damages during chemotherapy. The present study ventures to evaluate the natural flavonoid, Chrysin (5, 7-dihydroxyflavone) for its therapeutic immunomodulatory properties along with the chemotherapeutic drug, Cyclophosphamide (CP). Male Wistar albino rats were utilized for this study. Assays were conducted for Acute Toxicity, Hemolysis, Phagocytosis, Natural Killer (NK) cell cytotoxicity, and oxidative stress. RT-PCR, ELISA and Western Blot were performed to assess the expression of inflammatory markers. Assay results such as Phagocytosis Index (0.009 ± 0.001), NK Cell cytotoxicity (61.10 ± 4.99 %), expression of Perforin (0.45 ± 0.05 fold) and Granzyme (0.86 ± 0.01 fold), hepatic antioxidative enzymes GSH (27.75 ± 1.54 μg/mg), SOD (7.10 ± ± 0.35 U/mg) and CAT (249.06 ± 31.30 mM/Min/mg) and splenic hepatic antioxidative enzymes GSH (20.88 ± ± 0.74 μg/mg), SOD (7.10 ± 0.35 U/mg) and CAT (249.06 ± ± 31.30 mM/Min/mg) among the CP-treated groups were compared with those for the CP+Chrysin treated groups which were evaluated to be significantly increased with values of 0.016 ± 0.001, 82.73 ± 2.87 %, 0.77 ± 0.08 fold, 1.11 ± 0.02 fold, 47.60 ± 3.02 μg/mg, 08.97 ± ± 0.42 U/mg, 467.19 ± 15.92 mM/Min/mg, 29.02 ± ± 1.59 μg/mg, 5.17 ± 0.94 U/mg, 310.29 ± ± 9.1330 mM/Min/mg, respectively. Histopathological examination indicated that CP+Chrysin treated groups could recover from cellular damage triggered during the CP treatment. Results indicate the cytoprotective role of Chrysin, which in turn, could be reliably administered as a complementary therapy along with CP during chemotherapy.

Key words: *Chemotherapeutic agents, Cyclophosphamide, Chrysin, Inflammation, Toxicity.*

ЦИТОПРОТЕКТОРНИЙ ВПЛИВ ХРИЗИНУ (5, 7-ДИГІДРОКСИФЛАВОНУ) НА ТВАРИН, ЯКИМ ЕКСПЕРИМЕНТАЛЬНО ВВОДИЛИ ЦИКЛОФОСФАМІД

Хіміотерапевтичні препарати широко відомі своїми несприятливими побічними ефектами під час лікування онкологічних захворювань. Одним із додаткових підходів до вирішення цієї дилеми може бути використання природних сполук, які можуть оптимально протидіяти пошкодженню клітин під час хіміотерапії. Метою цього дослідження було оцінити природний флавоноїд, хризин (5,7-дигідроксифлавон), на предмет його терапевтичних імуномодулюючих властивостей у поєднанні з хіміотерапевтичним препаратом циклофосфамідом (ЦФ). У цьому дослідженні використовували самців-альбіносів мишей лінії Вістар. Було проведено дослідження гострої токсичності, гемолізу, фагоцитозу, цитотоксичності природних кілерів (ПК) та оксидативного стресу. Для оцінки експресії маркерів запалення було використано ПЛР-ЗТ, ІФА та Вестерн-блоттинг. Такі результати дослідження, як індекс фагоцитозу (0,009 ± 0,001), рівень цитотоксичності природних кілерів (61,10 ± 4,99 %), показники експресії перфорину (0,45 ± 0,05 разів) та гранзиму (0,86 ± 0,01 разів), антиоксидантних ферментів печінки, GSH (27,75 ± 1,54 мкг/мг), СОД (7,10 ± 0,35 од/мг) та каталази (249,06 ± ± 31,30 мкМ/хв/мг), а також антиоксидантних ферментів селезінки і печінки, GSH (20,88 ± ± 0,74 мкг/мг), СОД (7,10 ± 0,35 од/мг) і каталази (249,06 ± 31,30 мкМ/хв/мг) у групах, яким вводили

ЦФ, порівняли з показниками груп, яким вводили ЦФ+хризин. Було виявлено значні підвищення значень: 0,016 ± 0,001, 82,73 ± 2,87 %, 0,77 ± ± 0,08 разів, 1,11 ± 0,02 разів, 47,60 ± 3,02 мкг/мг, 08,97 ± 0,42 од/мг, 467,19 ± 15,92 мкМ/хв/мг, 29,02 ± 1,59 мкг/мг, 5,17 ± 0,94 од./мг, 310,29 ± ± 9,1330 мкМ/хв/мг, відповідно. Гістопатологічне дослідження показало, що групи, які отримували ЦФ+хризин, могли відновитися після пошкодження клітин, викликаного лікуванням за допомогою ЦФ. Результати показали цитопротекторну роль хризину, який можна вводити в якості надійної додаткової терапії у поєднанні з ЦФ під час хіміотерапії.

Ключові слова: хіміотерапевтичні препарати, циклофосфамід, хризин, запалення, токсичність.

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