石榴萃取之多酚（TMU023）造成人類神經膠質瘤細胞之死亡機制

A polyphenol extract (TMU023) from pomegranate induces cell death in human glioma cells

中文摘要

石榴（pomegranate）學名爲 Punica granatum 是石榴樹的果實。目前已知石榴可以造成細胞凋亡來抑制許多惡性癌細胞的生長，本論文利用從石榴萃取出的多酚物（polyphenol）— TMU023，來探討 TMU023 是否會造成 U87MG 神經膠質瘤細胞的生長抑制和細胞凋亡。實驗結果發現，TMU023 會抑制 U87MG 神經膠質瘤細胞的生長，使細胞的 cyclin E 表現增加，抑制 cyclin A 和 cyclin B 的表現，因而使細胞週期停留在 S 期。我們也發現 TMU023 會改變細胞中 Bax 和 Bcl-2 的比例，使的細胞色素 c（cytochrome c）離開粒線體，活化 caspase-9 造成 PARP 的斷裂而使細胞走向細胞凋亡。將 U87MG 神經膠質瘤細胞以 TMU023 處理之後，會活化 AMPK（AMP activated protein kinase）造成細胞自噬的細胞死亡，我們利用 chloroquine 來抑制細胞自噬，結果發現 chloroquine 可以保護 U87MG 神經膠質瘤細胞，避免因 TMU023 造成的細胞死亡。TMU023、AICAR（5-aminoimidazole-4-carboxamide riboside）和 metformin 都能活化 AMPK，增加 autophagosome 的形成使 LC3 被切割。我們結果證實 TMU023 會造成細胞的死亡是透過細胞凋亡和細胞自噬的途徑。

英文摘要

There are substances common as well as electrolyte can not detect by colorimetry method. Determination of Sodium, Potassium and Chloride can process by Flame Photometry、Atomic absorption spectrophotometry and Ion-Selective Electrode. Ion selective electrode is one kind of electrochemical half-reaction cell, its electrode potential varies with the ion concentration in the testing solution. It is used to measure the concentration of one specific ion in the solution. The electrolyte analyzer has been used as a practical ion concentration detect sensor because of its simplicity of device constructing, simple operation, high accuracy and precision. The ion selective electrodes are used in the clinical chemistry electrolyte analyzer to test the concentrations of sodium and potassium ion in the serum sample in Taiwan commonly. There are many hospitals applied Indirect Ion-Selective Electrode（Indirect ISE）clinical chemistry analyzer. Are there significant differences between Indirect ISE and Direct Ion-Selective Electrode（Direct ISE）？ Are the Direct ISE more accuracy routine clinical chemistry analysis method？ Are there some methods to eliminate the common interferences as well as lipid in routine serum sample？

We investigate the determination of sodium and potassium ion and focus on differences between Indirect ISE and Direct ISE in this thesis. We collect two hundred and thirty-three serum samples. Each sample splits into two aliquots. One aliquot process Indirect ISE electrolyte analysis and the other test by Direct ISE in Roche Integra and Hitachi clinical chemistry instrument. We get some results from this study：

1.There are significant differences between Indirect ISE and Direct ISE to analyze electrolyte. If the electrolytes are measured by Indirect ISE analyzer, there is a predictable decrease data results.

2.HDL-C and LDL-C two valuables have no significant correlations with differences between Indirect ISE and Direct ISE electrolyte analyzer. TG and T-cho two valuables have significant correlations with differences between Indirect ISE and Direct ISE electrolyte analyzer.

3.We apply organic reagent（Ethyl Acetate） to eliminate serum lipid and correct bias which from Indirect ISE analysis.

4.We apply ultracentrifuge method to eliminate serum lipid and correcte bias from Indirect ISE analyzer.

The results of this research shows the valuable mode in practical clinical chemistry field. Because this research is only small scope initial study about ISE, samples are minor and only apply one kind of clinical chemistry analyzer. We can not get a better precise score. As a consequence and extinguish predicting model is set up for clinical chemistry analysis field increasing personal health and clinical diagnosis abilities.