Doctoral Dissertation Abstract...

STUDIES ON THE ARTIFICIAL SWEETENERS ADDED TO THE SOME FOODS

Saime KÜÇÜKKÖMÜRLER, Supervisor: Assoc. Prof. Dr. Aysel BAYHAN, Department of Food Analysis, Faculty of Pharmacy, Gazi University, 06330 Ankara, Turkey
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This study was planned foundation and supported by the Gazi University Research foundation (1993-1995) and was carried out to determine whether the artificial sweeteners saccharine, cyclamate and aspartame are added to sweet foods, and how much they are included in diet foods as well as sweet foods.

We have studied the samples of jam, marmalade, squash, soft drinks, sweetmeat, baklava (sweet pastry) which are produced by 21 different firms and are on the market in Ankara. We have examined the quantity of cyclamate and saccharin included in these products. However these sweeteners cannot be seen in the food mentioned above. Three hundred samples have been examined in terms of sweeteners.

Aspartame was used in soft drinks between the rates 219.97 ± 7.04 - 560.16 ± 8.53 mg determined by spectrophotometric method. However it was seen that "aspartame" was used in non-diet soft drinks at the level of about 41.76±3.58 mg/lt. The aspartame used in diet soft drinks is not above the quantity proposed by Turkish Food Additives Regulations. Nevertheless the quantity of aspartame was used in two products according to the quantity written on the labels whereas the quantities in the other two products were over the labeled quantity ($p<0.05$).

According to the questionnaire for the consumers having diet foods we can easily say that 63 percent of aspartame such as table-top sweeteners has been preferably. It has been observed that table-top sweeteners are always consumed over the normal doses. Moreover, diet soft drinks are willingly and preferably used in the community. However, diet jam and marmalade are less consumed. Types of diet foods are limited in number.

INVETIGATION OF POSSIBLE ROLE OF OXYGEN-DERIVED FREE RADICALS ON DIGOXIN INDUCED ARRHYTMIAS IN ANAESTHETIZED GUINEA-PIGS

Mustafa ARK, Supervisor: Prof. Dr. İlkel KANZIK, co-Adviser: Assoc. Prof. Dr. İclal ÇAKICI Department of Pharmacology, Faculty of Pharmacy, Gazi University, 06330, Ankara, Turkey
Date of Defense : April, 16, 1997

In the present study, the role of oxygen-derived free radicals on digoxin (0.6 mg/kg, i.v. bolus injection) induced arrhythmias in anaesthetized guinea-pigs was investigated.

Guinea-pigs (300-400g) of either sex were anaesthetized with urethane (1.5 g/kg, i.p. injection) and electrocardiograms (ECG), mean blood pressure, heart rate and arrhythmias were recorded starting 30 min before digoxin administration and continuing for 60 min afterwards.

The potent antioxidant and superoxide scavenger, ascorbic acid (10-20 mg/kg, i.v. bolus injection, 10 min before digoxin administration), did not change arrhythmia parameters or haemodynamies.

The superoxide scavenger, superoxide dismutase (SOD) (30.000 U/kg, i.v. bolus injection, given 10 min before digoxin) and catalase, a hydrogen peroxide scavenger (15.000 U/kg, i.v. bolus injection, given 10 min before digoxin) given in combination, reduced the mortality rate from 86.7% to 50.0%. Desferrioxamine, a specific hydroxyl radical scavenger (10 mg/kg/h, i.v. infusion; starting 30 min before digoxine administration and maintained throughout the experiments) only reduced the incidence of ventricular fibrillation (VF) significantly (from 50.0% to 0.0%). Haemodynamics were not affected by desferrioxamine administration.

Dimethylsulfoxide (DMSO), a specific hydroxyl scavenger (4-40 mg/kg, i.v. bolus injection, given 5 min before digoxin administration) reduced the incidence of VF, (from 50.0% to 25.0%) but this reduction was not statistically significant.

Glutathione (10 mg/kg, i.v. bolus injection, given 5 min before digoxin) or N-acetyl-L-cysteine (20 mg/kg, i.v. bolus injection, given 10 min before digoxin) changed none of the arrhythmia parameters. However, glutathione (caused an elevation of mean arterial blood pressure) at 20 and 30 min and, N-acetyl-L-cysteine at 30 min after digoxin administration, significantly.

Results showed that direct association of free radicals with digoxin arrhythmias has been difficult to establish in vivo, because of a number of complicating processes, although free radical production might be increased during digoxin-induced arrhythmias.

STUDIES ON ASPERULA TAURINA L. Subsp. CAUCASICA (Pobed.) EHREND

Ufuk ÖZGEN, Supervisor: Prof. Dr. Maksut COŞKUN, Department of Pharmacognosy, Faculty of Pharmacy, Ankara University, 06100, Ankara, Turkey.
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Asperula taurina subsp. caucasica is growing in North Anatolia. The plant consist of a reddish underground part and there is no research carried out on this subspecies.

The botanical studies on this plant has been classified into two groups. First of all, plant was investigated morphologically in which general appearence has been drawn. After that the underground part of the plant was studies anatomically in the horizontal and vertical sactions.

In the chemical studies; test reactions for main compounds, identification, extraction, isolation and structure elucidation methods were applied to undergorund parts of A. taurina subsp. caucasica.

Classical test methods were used for screening the main active principles on whole plant. The amount of total antraquinone and mollugin were determined by spectrophotometric and High Pressure Liquid Chromatographic methods.

Quantitative determination was carried out by spectrophotometric and reversed-phase HPLC methods. The extinction of the extract which was prepared from the powdered underground parts of the plant, has been measured at 530±2 nm in order to determine the amount of antraquinone and total antraquinone. The amount of mollugin in the plants was determined by the method of reversed phase HPLC followed by obtaining the Mollugin's calibration curve. Quantitative determination of mollugin has been done on the two extracts which were prepared in maseration and Soxhlet apparatus.

Two different methods found in literature have been applied to prepare the extracts in which the 6 compounds were isolated (Compound I, II, III, IV, V and VI). TLC and HPLC methods have been used to determined the purity of certain isolated compounds (I, II, III and IV).

The structure of Compounds I and II were elucidated as mollugin (compound I) and β-sitosterol (compound II) respectively. The extensive studies have shown that the compound V might be glucose and studies for the last three compounds (compound III, IV,VI) are still in progress.

Keywords: Asperula, Rubiaceae, Mollugin, β-Sitosterol, HPLC

ERYTHROCYTE MEMBRANE AND LIPID PEROXIDATION IN STZ-DIABETIC RATS

Ş. Onur BOZKURT, Supervisor: Prof. Dr. M. Kutlay BURAT, Department of Biochemistry, Faculty of Pharmacy, Ankara University, 06100, Ankara, Turkey.
Date of Defense : June, 12, 1997

Free radical-mediated oxidation of biological molecules, membranes and tissues are accepted to be related with a variety of pathological events, including atherosclerosis, diabetes mellitus, inflammatory diseases, cancer and aging. The oxidation of membrane lipids has been implicated as one of the primary events in the oxidative cellular damage. The most important effect of free radicals is lipid peroxidation which causes oxidative modification of LDL and this ultimately results in the formation of atherosclerotic lesions. Circulating erythrocytes are also susceptible to oxidative damage as they are exposed to high partial pressures of oxygen, have membranes rich in polyunsaturated fatty acids and contain large amounts of iron that can potentiate free radical reactions. The biological effects of free radicals are controlled in vivo by a wide range of antioxdants such as vitamins E and C, carotenoids, glutathione and antioxidant enzymes such as catalase, superoxide dismutase and glutathione peroxidase. Reduced antioxidant defense status of plasma and erythyrocytes might result in increased peroxidation of cell membrane lipids and hence increased concentrations of lipid peroxides. Thus, monitoring oxidative state might play an important role in preventing diabetic patients from atherosclerosis. The purpose of our study is to investigate whether the susceptibility of LDL, red blood cell membrane and liver plasma membrane to oxidation is altered and if there is a correlation between the susceptibility of erythrocytes to oxidation and the peroxidation state of tissues, LDL and plasma membrane in STZ-diabetic rats. For this puspose, we measured the lipid peroxide leves of brain, liver, heart, lung, kidney, plasma, erythrocytes, low density lipoproteins, activities of superoxide dismutase, catalase, liver plasma membrane Na-K ATPase, plasma levels of vitamin C and vitamin E, oxidizability of eryhthrocyte membrane, low density lipoproteins and liver plasma membranes in 4, 8, 10, 16 week diabetic and 4 week vitamin E treated diabetic rats. The results of our experiments show that streptozotocin-diabetic rats had elevated lipid peroxide levels in tissues such as liver, kidney, brain, lung, heart, plasma, erythrocyte membrane, low density lipoproteins and diminished levels of antioxidant components such as vitamin E, vitamin C, and activities of superoxide dismutase and catalase ($p<0.001$). Erythrocyte membrane, LDL and plasma membrane oxidizability were significantly higher for STZ-diabetic rats then those of controls ($p<0.001$). Four week of vitamin E treatment resulted in low peroxide levels of tissues such as heart ($p<0.05$), kidney ($p<0.001$), brain ($p<0.001$), as well as plasma ($p<0.001$), LDL ($p<0.01$) and erythrocyte membrane ($p<0.001$). Vitamin E treatment also caused to decreased susceptibility of erythrocytes ($p<0.001$), LDL ($p<0.001$), and liver plasma membrane ($p<0.001$) to oxidation comparing to the diabetic controls without affecting the antioxidant parameters but vitamin E levels ($p<0.001$). We have found positive strong correlation between the erythrocyte susceptibility to oxidation and the oxidizability of LDL and plasma membrane and lipid peroxidation in tissues and plasma. There were also negative strong correlation between oxidizability of erythrocytes and antioxidant parameters in blood. According to our results, increased susceptibility of erythrocytes to oxidation could be a strong indicator of lipid peroxidation and of antioxidant status in diabetics, and routine vitamin E treatment could be beneficial for protection of these patients from oxidative stress.