

Drugs of the Future

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the possibility that hypertensive effect of NPS 2143 is mediated by calcium channel activity.

The aim of present study was to determine if the infusion of felodipine, inhibitor of calcium channel, prevents the hypertensive effect of NPS 2143 in rats.

Male Wistar rats were anaesthetized with Thiopental and infused i.v. with saline supplemented with 3H inulin for GFR determination and in part of rats with felodipine (30µg/kg/h) throughout the experiment. After 1 h of infusion, at the time 0 of experiment, NPS 2143 was administered as a bolus (1mg/kg b.w.). Control group of rats received vehicle only. MAP was monitored continuously in carotid artery. Urine was collected from cannulated bladder.

Changes of MAP were compared in 4 groups of rats. (Group 1) NPS 2143 resulted in significant increase of MAP with the most effect 60 min after administration of calcilytic (112±4 to 127±5 mmHg) (n=9). (Group 2) In control group, that received vehicle infusion only, no significant changes of MAP were observed. (Group 3) Felodipine infusion induced marked decrease of MAP from 110±5 (at -80 min) to 92±3 (at 0 min) and to 87±4 mmHg at 60min of experiment (n=8). (Group 4) In the presence of felodipine infusion, NPS 2143 administration did not increase MAP: 94±3 (at 0 min) to 95±5 mmHg 60 min after calcilytic administration (n=7).

We conclude that activity of calcium channels might mediate the increase of blood pressure induced by calcilytic NPS 2143 infusion in rats.

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PA-85

The oxidative status in depression after fluoxetine treatment

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Depressive disorder is still a rising and important problem in the modern world. It has resulted in a large variety of studies that target to determine molecular and neurochemical effects being a background of depression. The last decade studies paid attention to the theory different from monoaminergic hypothesis. One of this is the cytokine theory of depression, which has started to exist due to studies that showed the increased levels of pro-inflammatory cytokines and other markers of inflammatory process in depressed patients without any concurrent pro-inflammatory disease of known etiology. On the other hand, increased susceptibility to depression has been reported in patients with an elevated level of pro-inflammatory cytokines resulting from on-going inflammatory process. There is some evidence that an immunological system activation is related to the overproduction of reactive oxygen species (ROS), which can be adverse to lipids, especially lipid structure of the brain. Increased number of leucocytes and neutrophils which produce ROS may be decreased by selective serotonin reuptake inhibitors (SSRI).

The aim of this study was to determine the effect of fluoxetine on antioxidant enzymes and MDA levels in depressed patients and to compare these results with healthy people.

The study comprised of 50 persons treated due to depressive disorder. The control group consisted of 20 people.

The superoxide dismutase (CuZnSOD) activity in depressed patients before three -month treatment was 2084,80 U/Hb; after this period it was 2029,76 U/Hb. The catalase (CAT) activity in depressed patients before three -month treatment was 17,47U/Hb, after this period it was 17,64U/Hb. The glutathione peroxidase (GSH-Px) activity in depressed patients before three- month treatment was 73,80 U/Hb, after this period it was 70,78 U/Hb. The malondialdehyde (MDA) level in depressed patients before three- month treatment was 0.74µmol/Hb, after this period it was 0.60 µmol/Hb.

ROS are very important in the major depression but using SSRIs, like the fluoxetine, reduces the level of the free radicals because the activity of antioxidant enzymes returns to normal ranges as well as the level of the MDA.

PA-86

Small molecule sorption and desorption in and out of PAAm hydrogels at various temperatures

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Hydrogels are a unique class of polymeric materials which imbibe a significant amount of water into their internal molecular structure and maintain their permanent shape. The application of hydrogels to a variety of substrates leads to the production of thermoresistant coat-

ings, catheters and blood detoxicants. Hydrogels may be impregnated with biologically active agents, such as antibiotics, enzymes, contraceptives, drug antagonists, anticoagulants, and anticancer drugs and may serve as systems for the controlled release of the agents absorbed over a prolonged time period at a specific site of the body. Thus, one of the most potential applications of a hydrogel in pharmacy is the controlled drug-delivery system¹.

In this study, small molecule sorption and desorption in and out of PAAm hydrogels were studied by using steady state fluorescence (SSF) techniques. Pyranine was introduced as a fluorescence probe during polymerization. Fluorescence emission intensity, I_p from P_y was monitored for studying sorption and desorption processes at various temperatures. Scattered light intensities, I_{sc} from PAAm gel was also monitored to observed structural variations during sorption and desorption process. Sorption and desorption coefficients were produced by using Fickian diffusion model. Related activation energies were also calculated from the corresponding physical processes.

In addition, sorption, t_s and desorption, t_{sl} times produced at various temperatures are plotted in Fig. 1 versus temperature. It is seen that both t_s and t_{sl} values decrease as the temperature is increased, which indicates that both processes are shortened as the temperature is raised, as expected. However, sorption process decreases much faster than desorption process, indicating high response of the dried gel against penetrating small molecules at elevating temperatures.

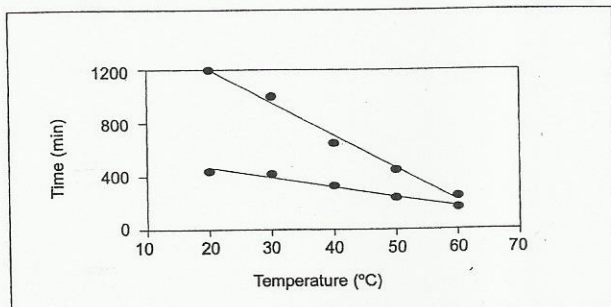


Fig.1. Plot of sorption, t_s and desorption, t_{sl} times versus temperatures

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PA-87

Slow release from carrageenan gels at various temperatures

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Carrageenan, a polymer widely used in food industry has been recently studied for its applications for controlled drug delivery [1]. Carrageenans are hydrophilic, high molecular weight, anionic linear heteropolysaccharides extracted from red algae. There are different types of carrageenans, but kappa (κ), iota (ι) and lambda (λ) are used for pharmaceutical applications. Both κ and ι -carrageenans have the ability to form gels but differ significantly in their rheological properties. Gels of κ type are hard, strong and brittle, whereas the ι -carrageenan forms soft and weak network structure [2,3]. κ -carrageenan has been used in the formulation of tablets [1,4] and hydrogels [5] containing ionic as well as nonionic drugs.

The aim of this work was to study slow release from kappa carrageenan gels at various temperatures by using steady state fluorescence (SSF) technique. Gels were prepared at 80°C with pyranine as a fluorescence probe. It was excited at 460nm during in situ slow release experiments and fluorescence intensities of the pyranine were monitored at 515nm as a function of time. Fluorescence spectra of pyranine at 40°C are presented in Figure 1. It was observed that fluorescence intensity decreased linearly as time was increased. A simple model consisting Case II diffusion kinetic was used to quantify the slow release experiments of kappa-carrageenan gels. It was observed that relaxation constant, k_o increased as temperature is increased. Activation energy was obtained and found to be 55.9 kJmol⁻¹ for the slow release process.

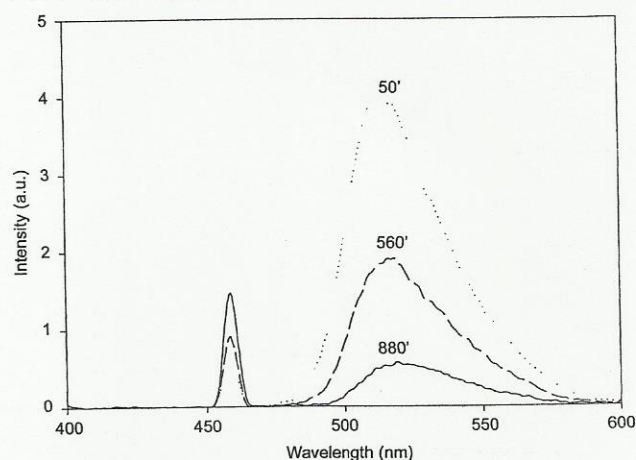


Figure 1. Fluorescence spectra of pyranine at 40°C

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