To our knowledge the e-Tox project represents the biggest approach to legacy data collection and sharing ever undertaken within the pharmaceutical industry. It is expected to set the ground for a major breakthrough in integrated in vivo toxicity prediction.

More information: www.e-tox.net.

doi:10.1016/j.toxlet.2010.03.838

P302-009
Analgesic effect of *Calendula officinalis* flowers extract in mice

N. Behtash[1], H. Shafaroudi[1], Z. Nazari Khorasgani[2]

[1] *Tehran Azad University of Medical Sciences, Tehran, Islamic Republic of Iran*, [2] *Ahvaz jondishapour University of Medical Sciences, Islamic Republic of Iran*

Due to the adverse effects of synthetic drugs there is a shift towards the use of medicine of herbal origin. It is documented that 80% of the world's population use natural remedies as alternative treatment. This widespread use of herb has prompted demands that herbal remedies be regulated as drugs to insure quality standards. *Calendula officinalis* is a common garden plant belonging to the Compositae family that its flowers are used medicinally. There is insufficient clinical evidence to support the use of that. Therefore in the present study calendula analegesic effect was studied. For this purpose hydroalcoholic extract of calendula flowers were prepared and evaluated for the analgesic activity using formalin and writhing test. In formalin test, groups of male Swiss mice (25–35 g, six in each group), were injected 20 μl of 2.5% formalin (in 0.9% saline) into the sub plantar space of the right hind paw and the duration of paw licking was determined 0–5 min (first phase) and 20–25 min (second phase) after formalin. 1 h prior to formalin injection test groups received orally different doses of plant extract (200, 400, 600 mg/kg). Control animals group received vehicle normal saline and morphine 2.5 mg/kg s.c.) pretreated animals were included in the study for comparison. In writhing test groups received orally different doses of hydroalcoholic extract (100, 200, 400 mg/kg) 1 h prior to an intraperitoneal injection of1% acetic acid in a volume of 1 ml/100 g. Indomethacin (2.5 mg/kg, p.o.) pretreated animals were used as positive control. The results showed that of calendula flowers extract, had significant.

doi:10.1016/j.toxlet.2010.03.839

P302-010
Effect of hydrophilic excipient on drug release from ethylcellulose and hydroxypropyl methylcellulose films containing lidocain and prilocain

M. Kouchak, S. Rezae, N. Moshabeh

Department of Pharmaceutics, Pharmacy School, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Islamic Republic of Iran

Transdermal delivery systems (TDS) by providing controlled release of drug and by passing hepatic first pass can increase bioavailability of drug and avoid systemic adverse effects. Lidocaine and prilocaine are amide-type local anesthetic agents which are used to minimize or in some cases eliminate pain from medical and Esthetic procedures. Applied topically to skin, causes a numbing effect that last for a few hours. The purpose of this study was to find methods to increase rate of drug release from different polymeric films containing lidocaine and prilocaine to obtain more rapidly effect. Several films containing lidocaine and prilocaine were prepared by using ethylcellulose (EC) or hydroxypropyl methylcellulose (HPMC) as basic films. The effect of propylene glycol, polyethylene glycol 4000 (PEG4000) as permeation enhancers and triacetin or dibutylphthalat (as plasticizer) on drug release properties were investigated. In vitro permeations studies were done using fransz diffusion cells and samples were analyzed by HPLC for each drug. The formulations were subjected to determine tensile strength, moisture absorption and content uniformity. Dibutylphthalate against triacetin played a dramatically effect on drug release rate and moisture absorption in HPMC films. The presence of propylene glycol on the formulations containing EC caused to increase the moisture absorption and drug release of the films but PEG4000 was not a significant effect on these variables in the HPMC films. The result of this research showed that the added hydrophilic materials (PEG4000, propylene glycol and triacetin) to an insoluble film (EC) acted as channeling agents and increased the rate of drug release. This was due to dissolving hydrophilic materials out of the film in dissolution medium and causing to create channels from which drugs can be released more rapidly and express immediate their anesthetic effects.

doi:10.1016/j.toxlet.2010.03.840

P302-011
Antidotal efficacy of bispyridinium oximes against nerve agents

B. Radic[1], S. Berend[1], A. Lucic Vrdoljak[1], D. Kukin[2], N. Fuchs[3], K. Kuca[4]

[1] *Institute for Medical Research and Occupational Health, Croatia*, [2] *University Hospital Center Rebro, Croatia*, [3] *Clinical Hospital "Sestre milosrdnice", Croatia*, [4] *Faculty of Military Health Sciences, University of Defense, Czech Republic*

Pyridinium oximes have been investigated for many years as compounds with a great potential in the treatment of organophosphorus compounds (OP) poisoning including insecticides and nerve agents. Oximes are known as reactivators of phosphorylated acetylcholinesterase (AChE), and they have beneficial antinicotinic effects in restoring activity of AChE. Atropine is favourable in the management of acute muscarinic signs and symptoms, and in combination with oximes, it is the treatment of choice for organophosphate poisoning. But there is still interest to develop new antidotes, and also to confirm the efficacy of those that are currently available. In this study in mice poisoned by soman, sarin, tabun and VX we tested the efficacy of three bispyridinium para-oximes with similar basic structure (KO27, KO48, K203) but differing in the linker between two pyridinium rings. In all experiments oxime in dose of 25% or 5% of its LD50 together with atropine (10 mg/kg) as therapy was used one minute after intoxication. Currently used oximes HI-6 and TMB-4 were included for comparison. The antidotal efficacy of tested compounds was expressed as protection index (PI) and maximal dose of poison (MDP).

Our experiments showed a relatively good efficacy of the tested oximes in sarin, tabun and VX, but lower in soman poisoning. Similar to HI-6 oxime, the best results with tested oximes were obtained in mice poisoned by VX. MDP was from 25 to 40 LD50 of VX, with survival of all experimental animals. Also, oximes K027 and K048 showed good antidotal efficacy of AChE inhibited by tabun. Their low toxicity is as much as beneficial effect in contrast to high toxicity of currently used TMB-4. It seems, that this results are in accordance with known protective and reactivating potential of pyridinium oximes.

doi:10.1016/j.toxlet.2010.03.841