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the absolute bioavailabilities were 41 ± 21 and 45 ± 5.9 % respectively suggesting a niotlerale first pass ettect.

80. Antiradical and antioxidative properties or steroid derivatives. V. Buko . 0. Lukivskaya[1], E. Naruta[1], A. Artsukevich[1], A. Maltsev[1]. H.-D. Tauschel [2]. W. Roemer [3]. D. Huebler [1]. M. Oettel [3]. [1]*Institute of Biochemistry. Grodno. Belarus.* [2]*Dr. Falk Pharma GmbH. Freiburg, Germany,* [3]*Jenapharm GmbH & Co. KG. Jena. Germany.*

We studied the in vitro and in vivo effects of steroid compounds. ursodeoxycholic acid (UDCA) and so-called "scavestrogen". 14 (Greek alpha). 15(Greek beta)-methylene-estra-1.3.5(10).8-tetraene-3.17(Greek beta)diol (JB11) on tree oxygen radicals and lipid peroxidation. A trap for hidroxyl radical (HR). POBN or tiron which is scavenger of superoxide radical (SR) were used as spin traps. UDCA led to the aapearance of the 2-fold lower signal of tiron-SR adduct and did not effect on the ESR spectra of HR-POBN adducls. We showed ihe signiricant inhibition of SR response in native liver microsomes at a concentration as low as 100 (Greek mu)M with maximal inhibition at 10 (Greek mu)M UDCA. The in vitro formation of tiron-SR adducls in the buffer and in microsomes in the presence of estrogens decreased as follows: J861 > 17lGreek alpha)-estradiol (17(Grcek alpha)-E) > 17(Greek beta)-estradiol (17(Greek beta)-E). In the experiment with UDCA. rats were treated with (Greek gamma)-irradiation (l Gy) for 24 h before decapitation. Two groups were twice treated with UDCA. 1 and 23 h after (Greek gamma)-irradiation (10 and 100 mg/kg, i.g.). UDCA normalized liver microsomal parameters enhanced by (Greek gamma)-irradiation: MDA. SR and carbonyls content. SOD activity, hydrogen peroxide production and chemiluminiscense attenuated by luminal or lucigenin. The UDGA dose of 10 mg/kg was not so ellective as the 100 mg/kg one. The antioxidative effect of 17(Grcek alpha)-E. 17(Greek beta)-E and J861 we evaluated in cholesterol-fed (200 mg/kg. 3 months) male rabbits. The esirogens (0.02 and 0.1 mg/kg. i.g.) were administered during the 2 last months. The cholesterol feeding increased the SOD activity. hydrogen and lipid peroxides production, SR. MDA and carhonyls content. NAD-PH-induced chemiluminiscence attenuated by lucigenin in the rabbit liver and serum. The estrogens decreased or normalized these parameters whereas the effect of J861 (0.1 mg/kg) was especially pronounced. We can conclude that steroid compounds such as UDCA. 17(Greek alpha)-E. 17(Greek beta)-E and J861 are quite ettective scavengers of free radicals and antioxidative agents.

81. Gamma-irradiation effects on biodegradable diclofenac sodium microspheres. S. Çalış, S. Bozdağ, M Tunçay, S. Ka.ş. A.A. Hıncal. *Hacettepe University,. Faculty of Pharmasy, Department of Pharmaceutical Technology. 06100, Ankara, Turkey.*

Biodegradable and hiocompatible polymers are currently used to provide controlled delivery of therapeutic agents mainly for parenteral administration. Therefore sterilization becomes an essential step in their formulalions. Gamma irradiation is the preferred technique for polymer-based biodegradable drug delivery systems whereas effects of γ-rays on biodegradable polymers are under investigation. The objective of present study was to evaluate the effects ot γ-irradiation on the physico-chemical properties of diclofenac sodium containing PLGA (50:50, MW 34 000 and 88 000) microspheres. Microspheres of PLGA at a copolymer ratio 50:50 and two different MW 34 000 and 88 000 were prepared by solvent evaporation technique. Afterwards they were irradiated at a fixed dose rate of 3.62 kGy/hr. at 0.5, 1.5, 2..5 MRad doses In vitro characterization of PLGA microspheres including drug loading, paticle size distribution. surface morphology and in vitro release were realized after the sterilization. There was not a significant change in drug loading value between irradiated and non-irradiated microspheres both for 34 000 and 88 000 MW. (16.10% non-irradiated. 16.21, 16.06, 15..94% for 0.5, 1..5, 2.5, MRad irradiated for MW 88 000 and 12.7% for non-irradiated 12.7, 12.7 and 12.6% for 0.5, 1.5, 2.5 MRad irradiated respectively for MW 34 000) but the difference occurred on surface morphology especially for 2.5 MRad irradiated microspheres. which was detected as the deformation on the surface. An increase in the released amount was observed for 2.5 MRad irradiated formulation: at the end of 24 hr release was about 36% from non-irradiated microspheres while it was determined as 46% from 2.5 MRad irradiated.

As a result, sterilization by γ-irradiation of parenteral delivery systems of PLGA microspheres requires utmost care and evaluation.

82. A mouse model to assess the efficiency of mucoadhesive particulate systems in the antibiotic treatment of *Helicobacter pylori* infections. C. Martinelli [1]. F. Ferrari [1]. L. Favalli [2]. C. Caramella [1]. *Department of Pharmaceutical Chemistry,* [2] *Institute of Pharmacology, University of Pavia, Pavia,. Italy.*

Paniculate mucoadhesive systems have recently been proposed by our group for the antibiotic site-specific treatment of *Hp* infections. The therapeutic idea was to obtain formulations able to facilitate the intimate contact between the drug and the gastric mucosa. to be retained in the stomach tor longer time periods and therefore to assure a higher concentration of the drug at the site of action. Aim of the present work was to set up an in vivo model (a mouse model) to evaluate the mucoadhesive properties of such systems, either granulates or micro-spheres. containing various mucoadhesive polymers (sodium algituite, polyarylic acid. chitosan hydrocloride) and amoxicillin as model drug. A mouse-adapted strain of *Hp.* the Sydney strain (SS1). was orally administered to inbred female C57BL / 6 mice. The animals were dosed three times in a 5-day period with 0.1 ml of bacterial suspension (approximately 10^9 organisms/ml). Bacterial colonization wa.s ensured hy positive reaction in the urease assay and by direct phase microscopy of mucus scrapings. The infected mice were divided into groups and treated as follows: pure amoxicillin solution (100 mg / kg) or watery suspensions of each mucoadhesive formulation (equivalent to 100 mg/kg amo.xicillin). The treatment was repeated daily tor 2 weeks. Animals were killed 24 h and 4 weeks alter the completion of therapy to assess clearance and eradication, respectively, of the bacteria. The level of colonization was determined by histology of the stomachs and viable counting of the bacteria. Significant differences were observed in both clearance and eradication grading of the treated mice in comparison with the controls (no treatment). As for the comparison between the treated groups, the mice administered with the mucoadhesive formulations showed higher grading of clearance and eradication than those receiving the pure amoxicillin solution.

83. Modelling the kinetics of release of octreotide from long-acting formulation in rabbits. E. Comets [1], F. Mentre [1], F. Nimmerfall [2], R. Kawai [2], P. Marbach [2], J. Vonderscher [2], [1] *Inserm U 436. CHU Pitié-Sulpétrière. 91 Bd tie I'Hospital. 75 013 Paris, France.* [2] *Novartis Pharma AG. Basel CH-4002. Switzerland.*

The lone-acting release formulation OncoLAR based on polymeric microspheres was developed to deliver octreotide. an octapeptide analogue of somatostatin. In this study, we developed a model to describe the processes of release yielding the complex concentration versus time profile observed after intramuscular (IM) administration of OncoLAR .

Kinetic data was obtained from 8 rabbits. They received 5 $mg.kg^{-1}$ IM of OncoLAR. and 26 blood samples were taken over 49 days. Concentrations of octreotide were assayed by radioimmunoassay.

The disposition model was fixed according to previous analyses. The triphasic release into the muscle was described with three successive models: the absorption from the muscle into the blood followed a first-order process. For each phase, several models were compared using the Akaike criterion after estimation by non-linear regression.

The drug burst, at the beginning of the release, was found to follow an exponential model. During the second phase, drug escaped the matrix through a diffusion process that was best described using a semi-empirical non-fickian model. The third phase, staning between day 7 and day 12. followed a Weibull sigmoid model. It was estimated to account