

DOCTORAL DISSERTATION ABSTRACTS

PREPARATION OF NONSTEROIDAL ANTIINFLAMMATORY OPHTHALMIC INSERTS

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In this study, we intended to prepare ophthalmic inserts of water-insoluble Indomethacin and water-soluble Ketorolac tromethamine.

Soluble ophthalmic inserts of these drugs were prepared using water-soluble polymers such as HPC, MC, HPMC and PVA by the film casting and compression molding methods. The ophthalmic inserts being nonsoluble in water were also prepared using hydrogels [poly (2-hydroxyethyl) methacrylate, poly (2-hydroxypropyl) methacrylate etc.]. Hydrogels are water-insoluble polymers that have the ability to swell in water.

The drug contents, the values of swelling degree, increase in weight and hydrophilicity of inserts were determined. The effects of these parameters on drug release were examined.

Ophthalmic inserts must be sterilized before they can be used. Therefore, inserts were sterilized by the gamma irradiation. The inserts were exposed to two different radiation doses and the effects of radiation doses on the drug stability and drug release from inserts were investigated.

As a result, the drug release over the period designed as 6 hours was observed from water-soluble inserts prepared by both methods for Indomethacin while this was achieved for Ketorolac tromethamine inserts prepared by compression molding method. The drug release over the time intended was also ensured for hydrogel inserts of both drugs.

It was concluded that two different radiation doses could be applied for the sterilization of inserts without changing in drug release and stability.

ASSESSMENT OF POSSIBLE CHANGES ON SOME IMMUNE PARAMETERS IN MAN CHRONICALLY EXPOSED TO LEAD AND CADMIUM

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In this study, some immunological parameters in workers occupationally exposed to inorganic lead and cadmium has been investigated and compared with that of non-exposed, age and sex-matched controls.

Blood and urinary lead and blood cadmium concentrations were determined with a graphite furnace atomic absorption spectrophotometer. They were found to be high in the exposed group compared with that of the control group. The difference was statistically significant. δ -ALA levels were determined with a UV-visible spectrophotometer. The difference between the levels of exposed and non-exposed groups were statistically significant.

An immunological assessment was made of the proliferation capacity of peripheral blood lymphocytes to respond to the specific mitogen PHA, a correlate of T-cell function, and to spontaneously lyse cell line of the K562, a measure of NK cell function. In neither case, was there a difference between exposed and control populations and no correlation between these parameters and blood lead concentration.

In addition, concentrations of some important cytokines in the serum were measured by ELISA method. Serum IL-1 levels were suppressed in the lead and cadmium exposed groups. While IL-2 and α -TNF levels were found to be normal, δ -IFN levels were suppressed in the lead exposed and enhanced in the cadmium exposed groups. The difference for IL-1 and g-IFN levels between exposed and control groups were statistically significant, but no correlation between blood lead and cadmium levels and serum cytokine concentrations were observed.

DOCTORAL DISSERTATION ABSTRACTS.....

THE APPLICATION OF GENOTYPIC MUTATION ANALYSIS TO THE STUDY OF ENVIRONMENTAL TOXICOLOGY

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Most of the currently available mutation systems depend upon the detection of a small fraction of mutated cells with a selectable mutant phenotype and thus these systems are limited to mutational analysis in only a few genes. The Restriction Site Mutation (RSM) assay has been developed for the detection of base changes which occur within restriction endonuclease recognition sequences. The RSM assay can be used to detect mutations in any gene for which DNA sequences are known without selection of a mutant phenotype. The RSM assay is based upon the isolation of resistant restriction endonuclease recognition sequences by using restriction enzymes and amplification of surrounding sequences with the Polymerase Chain Reaction (PCR). The study presented here covers the development and application of the RSM assay for detection of mutations induced by the environmental genotoxins, 7,12-dimethylbenz [a] anthracene (DMBA), N-Methyl-N-nitrosourea (MNU) and tobacco smoke, in vivo in the laboratory rat. 13 restriction endonucleases and primer pairs were identified as being suitable for the detection of mutations in the ras and p53 genes of the rat. Insensitive RSM products were detected in the 5' restriction endonuclease recognition sequences either by the direct alkylating agent MNU or by metabolically activated DMBA using the RSM assay. G to A and A to G transitions were identified in these restriction endonuclease recognition sequences in DNA extracted from a number of different tissues from treated animals. In order to achieve reliable and absolute quantitation of resistant restriction endonuclease sequences an internal standard method was introduced to the RSM assay.

The possible correlation of the presence of ras gene mutations in human oral tumours was investigated using PCR and direct sequencing. No mutations were found at codons 12, 13 and 61 of the K-ras, H-ras and N-ras genes in the DNA extracted from the human oral tumours.

PHARMACOGNOSIC RESEARCHES ON ESSENTIAL OILS OF PINUS SPECIES IN TURKEY

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The genus *Pinus* is represented by five species in Turkey. Among these species only *P. brutia*, *P. nigra* and *P. sylvestris* are used to produce timber by the Forestry Department in Turkey, while other parts are not utilized.

The purpose of this research was to study the volatile constituents of these three *Pinus* species as a Forest by-product. For this purpose, the needles of these species were periodically collected from the provinces of Antalya, Bursa, Denizli, İçel, Kastamonu, Kütahya, Muğla, Samsun and Sinop, which are located in different parts of Anatolia.

The composition of volatile oils was analyzed by means of GC and GC/MS and components were characterized using MS-Library search and the occurrence of a high ratio of monoterpenic hydrocarbon compounds was determined in the essential oils.

Forty-seven constituents are identified in the essential oils of *P. brutia*. The percentage of these constituents are as follows: α -pinene (% 10.98-33.45), β -pinene (% 8.60-51.97), Δ^3 -carene (% 0.05-11.45), β -caryophyllene (% 2.95-10.87), germacren-D (% 2.26-17.63).

Forty-two constituents are identified in the essential oils of *P. nigra*. The percentage of these constituents are as follows: α -pinene (% 4.51-49.63), β -pinene (% 1.15-34.10), β -caryophyllene (% 5.26-21.48), germacren-D (% 1.81-21.38).

Forty-three constituents are identified in the essential oils of *P. sylvestris*. The percentage of these constituents are as follows: α -pinene (% 19.44-56.88), β -pinene (% 2.87-17.09), camphene (% 0.44-16.84).

This is the first detailed report on the volatile constituents of the needles of *P. brutia*, *P. nigra* and *P. sylvestris*. In addition we defined that except in one or two provinces, these three *Pinus* species give volatile oil in high yield and good quality. According to the results of this study and the references, we can accept that *P. brutia* belongs to 'Chemotyp B' and *P. sylvestris* to 'Pinene Groups'. However, we could not evaluate *P. nigra* while the varieties and subspecies of the plants are not indicated in the references from other countries, but the amount of pinene is high in these species.