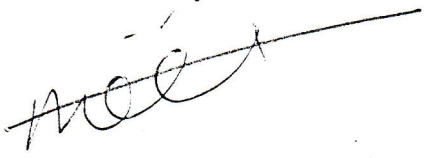
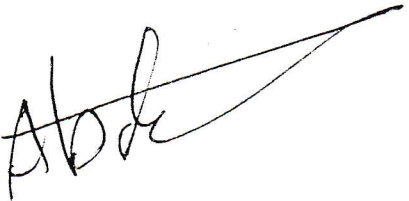


We the examining committee, certify that we have read this thesis entitled " Studies on the effects of some non - steroidal antiinflammatory drugs (NSAIDs) on granulocyte activity : Pattern of response and clinical applications " and have examined the student **ASIA SELMAN ABDULLAH** in its contents , and that in our opinion it is accepted as thesis for the degree of master of Science in Pharmacology .


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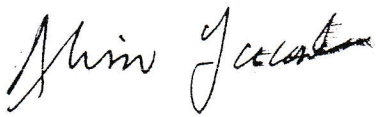

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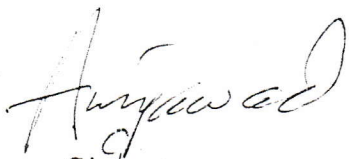

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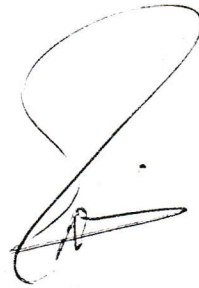
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We, hereby , certify that this work was carried out under our supervision at the department of pharmacology , College of Medicine , University of Basrah , as a partial requirement for the degree of master of Science in pharmacology .



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In view of the available recommendations , I forward this thesis for debate by the Examining committee.



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ABSTRACT

Non-steroidal antiinflammatory drugs (NSAIDs) were studied for their in vitro effects on human polymorphonuclear leucocytes (PMNs) activity as measured by luminol-dependent chemiluminescence of the whole blood with the aim of defining the well known variability in response to these drugs and in an attempt to search for a predictor(s) of such variability. This variability and related aspects of the use of NSAIDs in clinical practice were also investigated from doctor and patient perspectives.

Ninety normal subjects, 26 specialist doctors and 44 patients with osteoarthritis were involved in this study.

There is marked inter- and intraindividual variation in CL response to indomethacin (10 $\mu\text{g/ml}$), aspirin (300 $\mu\text{g/ml}$), ibuprofen (25 $\mu\text{g/ml}$) and diclofenac (8 $\mu\text{g/ml}$) added in vitro. The variation exhibited a continuous pattern. No statistically significant correlation was found between the effects of one NSAID and the other three drugs, nor between the effects of each drug and factors like age, sex, weight, height, PCV, Hb% and WBC count. Increasing the number of subjects from 40 to 90, did not alter the pattern of variability. It rather, clarified the role of Hb-type. Subjects with Hb-AS type responded mainly by enhancement to indomethacin and diclofenac, and by inhibition to Ibuprofen and aspirin. This could have an important clinical implications, if proved to be true. Another significant correlation was found with the type of blood group, when the number of subjects rather than the average net effect was compared. Subjects with blood group A and AB showed chemiluminescence responses towards enhancement compared to other blood groups.

A consistent pattern of enhancement and inhibition was evident . Enhancements and inhibitions by any two drugs involve a seemingly constant proportions of subjects . After exclusion of Hb-AS subjects, around 55% of subjects showed inhibitory CL response to indomethacin .

Drugs frequently prescribed by doctors or used by osteoarthritic patients, are ibuprofen, indomethacin and diclofenac . Ibuprofen 200 mg tablet seems to be the preferred formulation . Aspirin which was frequently prescribed by doctors, was not favoured by patients, while physicians tended to prescribe paracetamol more frequently than surgeons. Variation in response to NSAIDs appears to be well known to the doctors . They relate this phenomenon to factors inherited in the subjects, different manufacturers and to the type of disease, and also to subjective characteristics like age and sex . A good percentage of specialists used multiple NSAIDs to the same patient and the duration of use, for analgesic and antiinflammatory effects varies widely . The adverse effects are generally similar to what is already established, but doctors reported a high percentage of adverse effects, though of occasional occurrence, such as hypersensitivity reactions, acute renal failure and high blood urea .

It can, finally, be concluded from this study that Luminol-dependent CL responses to PMN activity is a good in vitro model to study the variability in response to NSAIDs . Characteristics of each individual cannot predict the pattern of variability, and HbAS subjects seem to be an interesting area for research in future . Several points in clinical practice need to be clarified such as multiple NSAID prescriptions and duration of therapy for analgesic and antiinflammatory activity.