



***Equivalent Intraperitoneal to Orally Administered Doses of
Ibuprofen on Dose Response Curve for Analgesia and
Prostaglandin Inhibitory Effect in Mice***

Thesis submitted for partial fulfillment of M.Sc. in Pharmacology.

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MB. BCh. 2009

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2015

Acknowledgment

I want to express my profound gratitude and sincere thanks to Prof. Dr. Sonia Salib for giving me the honour of working under her supervision, for her kind advice, guidance & continuous encouragement throughout the present work.

I want to express my profound gratitude and sincere thanks to Assistant Prof. Dr. May Hamza for her valuable supervision, for giving me much of her time and experience, for teaching me important laboratory skills, statistical analysis skills & important skills in thesis writing, for her kind continuous guidance, continuous encouragement and concern throughout the present work.

I want to express my profound gratitude and sincere thanks to Lecturer Dr. Nesreen El gayar for her valuable supervision, for her important advices in thesis writing , for her kind continuous guidance, valuable help and her persistent encouragement throughout the present work.

I wish to express my profound gratitude and sincere thanks to all my professors my senior staff and all my colleagues in the Pharmacology department, Faculty of Medicine, Ain Shams University for giving me much of their experience, great encouragement and helpful advices throughout the work.

I wish to express my profound gratitude and sincere thanks to lab assistant Mr. Ahmed Salama for the effort he had done and his accuracy throughout the work.

I would like to extend my thanks to all my family for their support and encouragement.

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List of abbreviations

AD	Alzheimer's disease
ADP	adenosine diphosphate
ANOVA	Analysis of variance
AUC	area under the curve
BCG	Bacillus Calmette-Guérin
BW	Body wieght
cAMP	Cyclic adenosine mono phosphate
CGRP	calcitonin gene-related peptide
COX	cyclooxygenase
coxibs	selective COX-2 inhibitors
CYP	Cytochrome P450 enzymes
DAG	diacylglycerol
DRG	dorsal root ganglia
ECM	extracellular matrix
EIA	Enzyme Immunoassay
ELISA	enzyme-linked immunosorbent assay
ERPF	effective renal plasma flow
GFR	glomerular filtration rate
i.p.	intraperitoneal
IC50	Inhibitory concentration
IL-1β	interleukin 1 β
IL-6	interleukin 6
IP3	inositol triphosphate
kD	kilodalton
LD	lethal dose

log	logarithm
LOX	lipoxygenases
NO	nitric oxide
NSAIDs	Non steroidal anti-inflammatory drugs
OTC	over the counter
PGE₂	prostaglandin E ₂
PGI₂	prostacyclin
PGs	prostaglandins
PKA	protein kinase A
PLC	Phospholipase c
PRB	pain related behaviour
S.C.	subcutaneous administration
S.E.M	standard error of the mean
S1P	Sphingosine 1-phosphate
SD	standard deviation
TNFα	tumor necrosis factor- α
TTX	tetrodotoxin
TX	thromboxane
vWF	Von Willebrand factor

Non steroidal anti-inflammatory drugs

For centuries, non steroidal anti-inflammatory drugs (NSAIDs) have been part of clinical practice. NSAIDs originally used as drugs with anti-inflammatory and analgesic effect, are now used for new therapeutic targets, some of which are unrelated to their primary mode of action. NSAIDs, as a group, have expanded to include a large number of compounds, supporting their efficacy in the treatment of different pathologies ranging from pain and inflammation to prevention and treatment of cancer (**Pountos et al., 2011**).

Hippocrates, the father of modern medicine, was the first to record descriptions of therapeutic benefits of extracts of willow bark and other plant sources of salicylates, 2400 years ago. He recommended chewing willow leaves for analgesia during labour and the juice of the poplar tree for eye diseases (**Mueller and Scheidt, 1994**). There was no real progress in the synthesis and use of NSAIDs until the chemical synthesis of salicylic and acetylsalicylic acids by Charles Gerhardt in 1853 and in 1897 by Felix Hoffmann (**Rainsford, 2007; Mullar and Scheidt, 1994**). Indomethacin and ibuprofen were developed in the 1960s. As ibuprofen is approved as over-the-counter drug, it is widely used (**Rainsford, 2007**). A large number of NSAIDs have been introduced in recent years and a second breakthrough in the

development of NSAIDs was the discovery of the cyclooxygenase-2 (COX-2) isoform and the development of the selective COX-2 inhibitors (coxibs) at the beginning of the 21st century (***Rainsford, 2013***).

Naturally, with the large number of NSAIDs in the market and post marketing surveillances, many of them have been withdrawn or have disappeared from the market (***Rainsford, 2013***). However, NSAIDs remain of the most commonly used medications, with approximately 70% of people aged 65 years or older are reported to use NSAIDs at least once per week (***Talley et al., 1995***). In the US alone, prescriptions for NSAIDs exceed 111 million every year, with an approximate cost of \$4.8 billion (***Laine, 2001***).

Various types of NSAIDs

Despite the differences in their chemical structures, NSAIDs share many properties especially in their use as analgesics. For example, all NSAIDs have a ceiling effect that limits their efficacy in severe increasing pain. Studies failed to clearly classify NSAIDs in-terms of efficacy, since patient response to NSAIDs varies. In other words, if a patient does not respond to an NSAID, other NSAIDs can be tried. In most cases, the side-effects profile will determine NSAID selection rather than minor differences in efficacy (***Green, 2001***).