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Emerging options of therapy with Cyclooxygenase 2 inhibitors

Essay

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Walid kh. EzzEldeen

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List of Abbreviations

AA : Arachidonic Acid

Aβ42 : β-amyloid peptide 42

ACCF : American College of Cardiology Foundation

ACE : Angiotensin Converting Enzyme

ACEI : Angiotensin Converting Enzyme Inhibitors

ACR : American College of Rheumatology

ACR20: American College of Rheumatology 20% improvement criteria

AD : Alzheimer's disease

ADA : American Diabetes Association

ADC : Adenocarcinoma

ADM : Adenomatous hyperplasia

AF : Atrial fibrillation

AGE : Advanced glycated end-products

AHA : American Heart Association

AIA : Aspirin-intolerant asthma

AKI : Acute Kidney Injury

AMI : Acute Myocardial Infarction

List of Abbreviations

AR : Aldose reductase

ARBs : Angiotensin Receptor Blockers

ARF : Acute Renal Failure

AS : Ankylosing spondylitis

ASA : Aspirin

ATP : Adenosine triphosphate

ATL : Aspirin Triggered Lipoxins

AUC : Area under the Plasma Concentration-time curve

BBB : Blood Brain Barrier

BD : Behcet's Disease

BFGF : Basic Fibroblast Growth Factor

BMD : Bone Mineral Density

BMMSC: Bone Marrow Mesenchymal Stem Cells

CABG : Coronary Artery Bypasses Grafting

Caco-2 : Cancer Colon Cells

CHD : Chronic Heart Disease

CHF : Chronic Heart Failure

CI : Confidence Interval

CL/F : Apparent Plasma Clearance

C max : Peak Plasma Concentration

List of Abbreviations

CNS : Central Nervous System

COX : Cyclooxygenase Enzyme

COX-1 : Cyclooxygenase -1 Enzyme

COX-2 : Cyclooxygenase-2 enzyme

CRP : C reactive protein

CVS : Cardiovascular Disease

CYP2C9 : Cytochrome P450 2C9

DGR : Duodeno-Gastric reflux

DIE : Drug-induced esophageal injury

DILI : Drug Induced Liver Injury

DPN : Diabetic Peripheral Neuropathy

EECs : Endometrial Epithelial Cells

EULAR : European League Against Rheumatism

F : Oral bioavailability

FAP : Familial Adenomatous Polyposis

FDA : Food and Drug Administration

Fe : Fraction excreted in unchanged form into urine

Fu : Fraction of drug unbound in plasma

GCA : Giant-Cell Arteritis

List of Abbreviations

GI : Gastro-Intestinal

HIS : International Headache Society

Ig : Immunoglobulin

KYNA : Kynurenic Acid

LOX : Lipoxygenase

LTA4 : leukotriene A4

LTB4 : leukotriene B4

LTC4 : leukotriene C4

LTD4 : leukotriene D4

LTE4 : leukotriene E4

MMPs : Matrix Metalloproteinases

MI : Myocardial Infarction

NADPH : Nicotinamide adenine dinucleotide phosphate

NF-Kb :Nuclear Factor Kappa-light-chain-enhancer of activated B cells

NO : Nitric oxide

O_2 : Oxygen

OA : Osteoarthritis

PDGF : Platelet Derived Growth Factor

PG : Prostaglandins

List of Abbreviations

PGG2 : Prostaglandins G2

PGH2 : Prostaglandins H2

PGI2 : prostacyclin

PGD2 : Prostaglandins D2

PGF2a : Prostaglandins F2a

PGE2 : Prostaglandins E2

PLA : Phospholipase

PKa : Acid dissociation constant

PKC : Protein kinase C

POX : Peroxidase

PPI : Proton Pump Inhibitors

RA : Rheumatoid Arthritis

RAGE : Receptor for advanced glycated end-products

RCT : Randomized Control Trial

ROS : Reactive oxygen species

RR : Relative risk

SLE : Systemic Lupus Erythematosus

SNc : Substantia Nigra Pars compacta

SSRI : Selective Serotonin Reuptake Inhibitors

List of Abbreviations

T1/2 : Elimination Half Life

TIA : Transient Ischemic Attacks

Tmax : Time to maximum plasma concentration

tNSAIDS : Traditional non-steroidal anti-inflammatory drugs

TNFα : Tumor necrosis factor α

TNFi : Tumor necrosis factor-alpha inhibitors

TXA2 : Thromboxane A2

TXB2 : Thromboxane B2

ULN : Upper limit of normal

USPSTF : United States Preventive Services Task Force

Vss : Apparent volume of distribution at steady state

5-HPETE : 5-hydroperoxyeicosatetranoid acid

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Introduction

Cyclooxygenase (COX) enzymes mediate prostaglandin generation.COX-1 is expressed in all cells, producing prostaglandins that maintain cellular homeostasis, and COX-2 is an inducible enzyme that generates inflammatory prostaglandins at sites of inflammation and healing **(Mateos, 2010).**

Nonsteroidal anti-inflammatory drugs (NSAIDs) that non-selectively inhibit COX-1 and COX-2 continue to be an important option for management of pain. However, despite the potential advantages NSAIDs, including their opioid-sparing effect and reduced opioid-related side effects, improved analgesia, and attenuation of the inflammatory pain response; several side effects limit their use. NSAIDs predispose to ulcer formation and upper gastrointestinal bleeding, impaired coagulation, cardiovascular effects and renal dysfunction **(Mateos, 2010).**

A relatively frequent problem with the use of NSAIDs and/or aspirin, and less frequently with paracetamol, is the development of intolerance and hypersensitivity reactions, a situation for which diverse alternatives have been proposed. One of these includes the use of cyclooxygenase 2 specific inhibitors (coxibs) **(Bello and Niembro, 2009).**

Selective cox-2 inhibitors (coxibs) have been shown to possess much improved GI tolerability and reduced GI related