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**300 LEVEL MBBS FIRST PROFESSIONAL EXAMINATION 2018/2019 SESION**

**MARKING SCHEME FOR QUESTION ON PROSTAGLANDINS, THROMBOXANES AND LEUKOTRIENES**

**1(A)**

**Biosynthesis and Action of Prostaglandins**

Membrane bound phospholipids Cortisol (-)

Phospholipase A2 Epinephrine (+)

Arachidonic Acid Thrombin (+)

Cyclo-oxygenase Aspirin (-)

Prostaglandin G2 Indomethacin (-)

Peroxidase

PGI2 PGH2 TXA2

PGF2 PGE2 PGD2 Inactive PGs

Adenyl Cyclase

ATP Cyclic AMP Biological effects**. 4 MARKS**

Prostaglandins are derived from polyunsaturated fatty acids (PUFAs) as PGs are not stored as such; they are stored in membrane as phospholipids.

Arachidonic acid is then released from phospholipid by the action of phospholipase A2.

Synthesis of Arachidonic acid is catalysed by prostaglandin H synthase (PGHS) as it contains two enzyme activities, Cyclo-oxygenase and Peroxidase. PGG2 and PGH2 are then formed as intermediates during the synthesis of other PGs. Then specific enzymes convert PGH2 to other prostaglandins.

**2 MARKS**

**SYNTHESIS OF LEUKOTRIENES**

Arachidonic acid

5-lipo-oxygenase

5-hydro-peroxy-eicosa-tetra-enoic acid (5-HPETE) HETE

LTA Synthase

Leutotriene A2 LTC4

Glutamic acid

Leukotriene B4 LTD4 LTE4

Glycine **4 MARKS**

**1(B)**

Nonsteroidal anti-inflammatory drugs are a drug class that reduce pain, decrease fever, prevent blood clots and in higher doses, decrease inflammation.

NSAIDS prevent blood clots by inhibiting the action of Thromboxane A2 thereby preventing platelet aggregation that may form clots to cause heart attack.

Two types of NSAIDs have been differentiated

1. The selective
2. The Non selective.

Most NSAIDs are non-selective and they inhibit the activity of both COX-1 and COX-2. These NSAIDs while reducing inflammation also inhibit platelet aggregation especially aspirin and increase the risk of gastrointestinal ulcers or bleeds by blocking the COX-1 enzyme and distrupting the production of prostaglandins in the stomach. They cause ulcers by interfering with the stomach’s ability to protect itself from gastric acids while stomach acids are vital to the digestive process, they can cause damage if the protective barriers of the stomach are compromised.

Aspirin also increase the risk of kidney disease by inhibiting physiological COX-1 activity.

The most prominent NSAIDs are Aspirin, Ibuprofen, Naproxen, Indomethacin and Celecoxib.

Paracetamol on the other hand is not considered an NSAID, because it has only minor anti-inflammatory activity as it treats pain mainly by blocking COX-2 mostly in the central nervous system but not much in the rest of the body. **7 MARKS**

**Mechanism of action of Aspirin**

Aspirin causes several different effects in the body, mainly the reduction of inflammation to the prevention of clotting.

Aspirins ability to suppress the production of PGs and thromboxanes is due to its irreversible inactivation of the COX-enzyme.

It acts as an acetylating agent where an acetyl group is covalently attached to a serine residue in the active site of the COX-enzyme, thereby inhibiting it.

Aspirin is more specific for the inhibition of COX-2 than COX-1 and a side effect of aspirin mechanism is that the ability of the blood to clot is generally reduced and excessive bleeding may result from the use of Aspirin. **3 MARKS** **TOTAL MARKS =20**