AUTOCOIDS

Mr. D.Raju, M.pharm,
Lecturer

DEFINITION

An organic substance, such as a hormone, produced in one part of organism and transported by the blood or lymph to another part of the organism where it exerts a physiologic effect on that part.

TYPES OF AUTACOIDS:

- Amines : Histamine,5-Hydroxytryptamine.
- Lipids : Prostaglandins, Leukotriens,
- Platelet activating factor.
- Peptide : Bradykinin , angiotensin.

HISTAMINE

- SYNTHESIS AND DEGRADATION OF HISTAMINE

Histidine

↓ decarboxylase

Histamine → Imadazole acetic acid

↓ N-methyl transferase

N-methyl histamine

↓ oxidase

Methyl imidazole acetic acid

PHARMACOLOGY

H1	H2	H3
S.M - contraction	Gastric gland-acid secretions	Brain- inhibition of histamine release- sedation
B.V – vaso dilation	B.V-dilation	B.V - vaso dilatation
Afferent nerve ending - stimulation	Heart-postive inotropy	Skin , gastric, mucosa- decrease histamine release
Ganglionic cell- stimulation	Uterus - relaxation	Lungs , spleen – decrease histamine release
Adrenal medulla-release of CAs		
Brain - transmitte		

CLASSIFICATION

	H1	H2	H3
SELECTIVE AGONISTS	2-methylhistamine,2-pyridylethylamine,2-thiazolyl ethylamine	4-methy histamine, Dimaprit, impromidine	ά-methyl histamine
SELECTIVE ANTAGONISTS	Mepyramine, chlorpheniramine	Cimetidine, ranitidine	Thioperamide, impromidine
RECEPTOR TYPE	G-Protein coupled	G-P	G-P
EFFECTOR PATHWAY	IP3/DAG Ca+ release	C-AMP inc	Ca+ infulx ,K+ channel activation, cAMP dec

THERAPEUTIC INDICATION

- Common cold
- Motion sickess
- Duodenal ulcer(Zollinger - ellision syndrome)
- Parkinsonism
- Allergic disorders
- Sedative and hypnotic , Anxiolytic

ADR: CNS depression, fatigue, gynecomastia in men, galactorrhea women.

SEROTONIN

- Sertonin (vasoconstrictor) appeared serum .

SYNTHESIS

TRYPTOPHAN

↓ hydroxylase

5-Hydroxytryptophan

↓ decarboxylase

5-HT → (MAO) 5-Hydroxy indole acetic acid

↓ dehydrogenase

5-Hydroxy tryptohol

TYPES

RECEPTOR	LOCATION	MAIN EFFECTS	SECOND MESSENGER	AGONISTS	ANTAGONISTS
1A	CNS	Neuronal inhibition, Behavioural effects	cAMP	5-CT 8-OH-DPAT Buspirone	Spiperone, Methiothepin, Ergotamine
1B	CNS VASCULAR-S.M	Pulmonary vasoconstrion	cAMP	5-CT Ergotamine	Methiothepin
1D	CNS B.V	Cerebral vaso constriction, locomotion	cAMP	5-CT Sumatriptan	Methiothepin Ergotamine
2A	CNS PNS S.M PLATELETS	s.m contraction	IP3/DAG	ả-Me-5-HT LSD(CNS) LSD(Peripher y)	KETANSERIN, cyproheptadi ne
2B	GASTRIC FUNDUS	contraction	IP3/DAG	ả-Me-5-HT	-
2C	CNS	Cerebrospinal	IP3/DAG	ả-Me-5-HT	Methysergide

RECEPTOR	LOCATION	MAIN EFFECTS	SECOND MESSENGER	AGONISTS	ANTAGONISTS
5-HT3	PNS CNS	Neuronal excitation, emesis	ligand-gated cation channel	2-Me-5-HT, Chlorophenyl biguanide	Ondansetron,tropisetron
5-HT4	PNS CNS	Gi motility	cAMP	5-methoxy-tryptamine, metochlopromide	Various exp.comp
5-HT5	CNS	Not known	Not known	Not known	Not known
5-HT6	CNS	Not known	Not known	Not known	Not known
5-HT7	CNS, GI TRACT, B.V	Not known	cAMP	5-CT,LSD	Various 5-HT2

PHARMACOLOGY

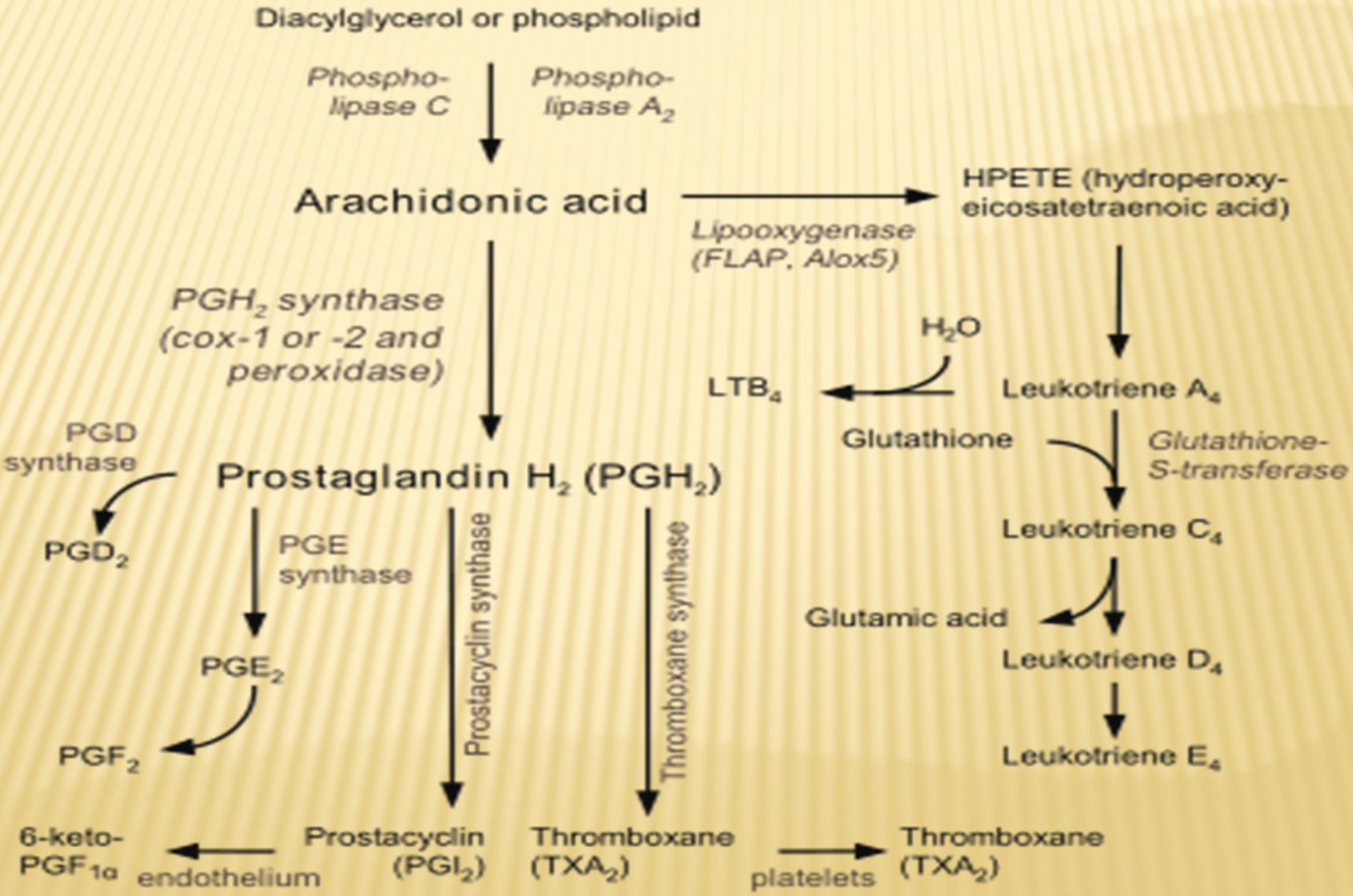
- CVS : Arteries are constricted as well as dilated by direct action of 5-HT.
- S.M : Stimualtor of GIT.
- GLANDS : It inhibits gastric secretion. It ulcer protective property.
- RESPIRATION: Hyperventilation
- PLATELETS : 5-HT cause change in shape of platelets and is a weak aggregator.

THERAPEUTIC USES

- 5-HT AGONISTS : Anxiolytics (Buspirone),
  Depression(Fluoxetine)
  Migraine(Ergot alkaloids)
- 5-HT ANTAGONISTS: Nausea, emesis, antineoplastic therapy (Ondansetron, Granisetron, Dolasetron)

ADR: Abdominal pain, Muscle cramps, Chest pain.

PROSTAGANDINS AND LEUKOTRIENES (EICOSANOIDS)



PHARMACOLOGICAL ACTIONS

ORGAN	PGE2	PGF2ά	PGI2	TXA2
B.V	Vaso dilatation	Vaso dilatation	Vaso dilatation	Vaso constriction
HEART	Weak inotropic, cardiac stimulation	Weak inotropic	–	–
PLATELETS	Variable effect	–	Anti aggregatory	aggregation
UTERUS	contraction	contraction	–	–
BRONCHI	Dilatation, inhibits histamine	constriction	Dilatation, inhibits histamine	constriction
STOMACH	Acid secretion(dec), Mucous production(inc)	–	Acid secretion(dec), Mucous production(inc)	–
INTESTINE	Contracts	spasmogenic	Weak	Weak

THERAPEUTIC USES

- PGE1 : CHF (Alprostadil)

  NSAID-induced GI ulcer (misoprostol)
- PGF2ά : Topically to lower intraocular pressure in glaucoma.
- PGI : pulmonary hypertension.(Flolan)

ADR :

Diarrhea , Hypotension, Flushing,

Cardiac Arrest , Anemia,

Menstrual irregularities , Abortion

Decreased renal function.

LEUKOTRIENES

- PHARMACOLOGY :

- CNS : fall in B.P
- S.M : Bronchoconstrictors and spastic contraction of GIT at low concentration
- AFFERENT : Carrying pain impulses and tenderness to inflammation.

THERPEUTIC USES

- TREATMENT OF ASTHMA (Zileuton)
- Reduced bronchospasm
- ADR :
- GI upset ,
- liver dysfunction