5-HYDROXYTRYPTAMINE AGONIST & ANTAGONIST

Non-Selective Drugs

• **Cyproheptadine**: It blocks 5 HT2A, H1 and muscarinic receptors. It increases appetite and can be used in children to promote weight gain.

• **Methysergide**: It is a 5 HT2A/2C antagonist and a 5 HT1 agonist. It is indicated for the prophylaxis of migraine attacks but prolonged use can result in pulmonary, endocardial and retroperitoneal fibrosis.

• **LSD**: It is an ergot derivative and a powerful hallucinogen. It acts as an agonist at several serotonin receptors including 5 HT1A, 5 HT2A/2C and 5 HT5-7 receptors

• 5-HT1B/D-receptor agonists (e.g. the triptans) are used for treating migraine.

• **5-HT2-receptor antagonists** (e.g. methysergide, ketanserin) act mainly on 5-HT2A receptors but may also block other 5-HT receptors, as well as α adrenoceptors and histamine receptors

Ergotamine and methysergide belong to the ergot family and have been used mainly for migraine prophylaxis (although methysergide is rarely used these days). **Other 5-HT2 antagonists** are used to control the symptoms of carcinoid tumours.

Ergot Alkaloids These are derived from a fungus *Claviceps purpurea*. Important compounds are ergotamine, ergometrine (ergonovine), ergotoxine, bromocriptine, dihydroergotamine and methysergide. These drugs **possess partial agonistic and antagonistic effect at 5HT, α and dopaminergic receptors**. These drugs are only α blockers that can cause vasoconstriction due to their partial agonistic activity on α and 5HT2 receptors (maximum with ergotamine). Hydrogenation of the compound decreases α agonistic activity but increases the α blocking potential. Therefore, dihydroergotamine has very little vasoconstricting activity. Ergot derivatives can cause dry gangrene of hand and feet as well as coronary vasospasm.

• Ergotamine and dihydroergotamine are used for the treatment of acute attack of migraine *or* migraine prophylaxis. These are contraindicated in patients with ischemic heart disease (due to their propensity to cause coronary vasospasm).

• Ergometrine, used in obstetrics to prevent postpartum haemorrhage

• Dihydroergotoxine (codergocrine) is useful for the treatment of dementia.

• Bromocriptine is useful in Parkinsonism, and endocrine disorders (hyperprolactinemia and acromegaly).

• Methysergide, formerly used to treat carcinoid syndrome, and prophylaxis of migraine attacks

	Actions at receptors					
Drug	**5-HT**	**α Adrenoceptor**	**Dopamine**	**Uterus**	**Main uses**	**Side effects, etc.**
Ergotamine	Antagonist/ partial agonist (5-HT_1) Antagonist (other sites)	Partial agonist (blood vessels)	Inactive	Contracts ++	Migraine (largely obsolete)	Emesis, vasospasm (avoid in peripheral vascular disease and pregnancy)
Dihydroergotamine	Antagonist/ partial agonist (5-HT_1)	Antagonist	Inactive	Contracts +	Migraine (largely obsolete)	Less emesis than with ergotamine
Ergometrine	Weak antagonist/ partial agonist (5-HT_1)	Weak antagonist/ partial agonist	Weak	Contracts +++	Prevention of postpartum haemorrhage (Ch. 36)	Nausea, vomiting
Bromocriptine	Inactive	Weak antagonist	Agonist/partial agonist	—	Parkinson's disease (Ch. 41) Endocrine disorders (Ch. 32)	Drowsiness, emesis
Methysergide	Antagonist/ partial agonist at several subtypes	—	—	—	Carcinoid syndrome Migraine prophylaxis (rarely used)	Retroperitoneal and mediastinal fibrosis Emesis

• **5-HT3-receptor antagonists** (e.g. granisetron, ondansetron, palonosetron) are used as antiemetic drugs, particularly for controlling the severe nausea and vomiting that occurs with many forms of cancer chemotherapy.

• **5-HT4-receptor agonists** that stimulate coordinated peristaltic activity (known as a 'prokinetic action') could be used for treating gastrointestinal disorders. **Metoclopramide** acts in this way, as well as by blocking dopamine receptors. Similar but more selective drugs such as cisapride and tegaserod were introduced to treat irritable bowel syndrome, but were withdrawn on account of adverse cardiovascular side effects