

**Q2 Classify the calcium channel blockers and provide one example of a drug for each class (20% marks). Compare and contrast the pharmacology of nimodipine and verapamil (80% marks) (March 2014, Q17 Sept 2011)**

**Class I** – Phenylalkylamines eg, verapamil

**Class II** – Dihydropyridines.

First generation - nifedipine

Second generation - felodipine

Third generation - amlodipine

**Class III** – Benzothiazepines eg, diltiazem

	<b>Nimodipine</b>	<b>Verapamil</b>
Description/indications	Nimodipine is a calcium antagonist that causes vasodilatation, it has a relatively specific effect on cerebral arterioles and it used in the management of SAH	Verapamil is a synthetic derivative of papaverine which acts as a calcium channel blocker. It is used in the management of HTN, supraventricular arrhythmias and angina.
Pharmaceuticals	Available in PO tablets (30mg) and IV solution 200mcg/ml	Comes in immediate or sustained release tablets of varying strengths and IV solution for injection
Pharmacodynamics	Binds to the N binding site of the L-type calcium channels on vascular smooth muscle to reduce intracellular calcium levels. Increases cerebral blood flow without any demonstrable steal effect.	Binds to the V binding site of the L type calcium channel. Reduces conduction in atrial, ventricular and purkinje cells, reduces cardiac contractility and also causes peripheral vasodilatation.
Side effects	Decreases SVR and can increase CO (overall may drop BP)	Dizziness, nausea, flushing, postural hypotension. In patients without CCF can improve cardiac function by improving ischaemia. In patients with CCF can make LV function worse (because it reduces myocardial contractility). Contraindicated in patients with WPW as may cause VT/VF
Pharmacokinetics		
- Administration	Route- PO or IV Dose - 60mg Q4H PO or 20mcg/kg/hr IV Bioavailability - well absorbed but high first pass metabolism so bioavailability 30%	Route - PO or IV Dose - from 40mg PO or 5-10mg IV Bioavailability - extensive first pass metabolism, bioavailability 25% Time to onset - minutes for IV, 1-2 hours PO
- Distribution	Vd 1-2L/kg Highly protein bound 98% Highly lipid soluble	Vd - 3.8L/kg Extensive protein binding 90%
- Metabolism	Demethylation and dehydrogenation to inactive pyridine analogue	Via hepatic enzymes. One active metabolite.
- Elimination	Inactive metabolites urine and faeces. Half life 2-4 hours	70% via urine (active and inactive metabolites), remainder in faeces. Half life 3-6 hours