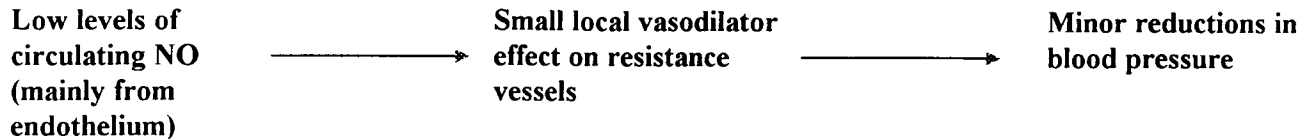
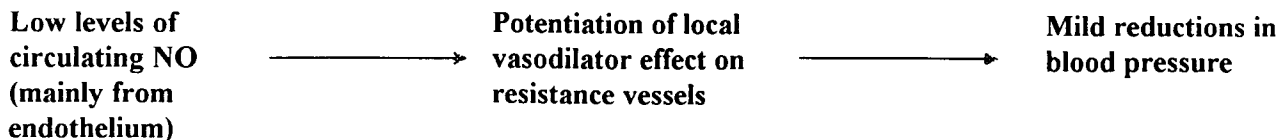


## Nitric Oxide and blood pressure control

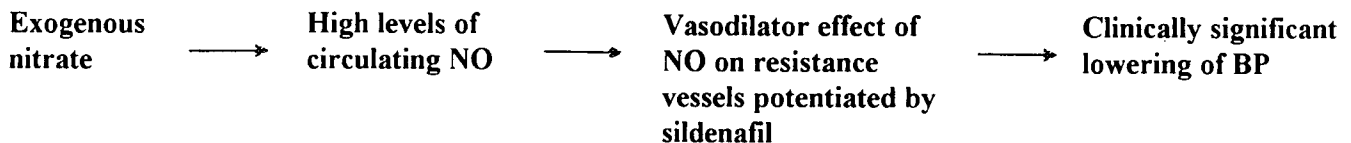
- Nitric Oxide (NO) is a widely distributed endogenous vasodilator. Sources of NO within the cardiovascular system include the endothelium and the peri-vascular nerve endings. Under physiological conditions, changes in vessel wall stress cause release of (mainly endothelial) NO. The circulating levels of NO are low and the molecule is labile; it acts locally at the site of release and modulates systemic vascular resistance, and therefore contributes to the control of blood pressure.



- Under physiological conditions the effects of sildenafil on blood pressure are only mild to moderate. These changes are not dose-related (in the dose range of 25mg-800mg) and are not normally associated with symptoms except for mild headache and facial flushing associated with dizziness.



- When patients take nitrate therapy, high levels of NO are present in the circulation. By inhibiting type 5 cGMP phosphodiesterase (PDE5) which is present in the vascular smooth muscle cells, sildenafil potentiates the vasodilatory effect of circulating NO, resulting in a significant fall in blood pressure.



## Combination of sildenafil and non-nitrate vasodilators

The potentiating effect of sildenafil on lowering of blood pressure in patients taking nitrate therapy is not observed with other vasodilator agents. Extensive safety data from phase II/III studies suggest that patients who take anti-hypertensive medication are not at higher risk of developing symptoms associated with lowering of blood pressure (e.g. dizziness) when they take sildenafil. This applies to patients who take calcium channel blockers, ACE inhibitors, a-blockers, b-blockers, diuretics as single or combined therapy for hypertension and/or angina.