When much longer duration of action is needed, oral preparations can be given that contain sufficient amount of drug to result in sustained systemic blood levels of the parent drug.

**Organ systemic effects:**

1. Vascular smooth muscle: All segments of vascular system respond with relaxation.
   - Arterioles and precapillary sphincteres are dilated least (less ability to release nitric oxide from the drug).
   - Primary direct result: marked relaxation of veins with increased venous capacitance and decreased ventricular preload.
     - Pulmonary vascular pressures and heart size are significantly reduced.
     - In the absence of heart failure cardiac output is reduced.
     - Orthostatic hypotension may be marked and syncope can result.
     - Compensatory responses may result in tachycardia and increased cardiac contractility (baroreceptors, hormonal mechanisms, renal mechanisms) * these compensatory mechanisms contribute to tolerance.


3. Other effects:
   - Reacts with hemoglobin to produce methehmoglobin (not significant in therapeutic doses but can cause pseudocyanosis, tissue hypoxia and death in overdosage).

**CALCIUM CHANNEL BLOCKING DRUGS:**

- Transmembrane calcium influx is necessary for the contraction of smooth and cardiac muscle.
  - Blocking the influx causes long lasting relaxation in smooth muscles.
  - Cardiac muscle: decreased contractility; decrease sinus node pacemaker rate.

**Organ system effects:**

- Smooth muscle: Vascular smooth muscle are most sensitive but relaxation may also be seen in brochiolar, GIT, and uterine smooth muscles.
  - Arterioles are more sensitive than veins.
  - Orthostatic hypotension is not a common adverse effect.
  - Blood pressure is reduced.
  - Cardiac muscle: highly dependent on calcium influx for normal function.
  - Reduce cardiac contractility in a dose dependent fashion.
  - In some cases CO may also decrease.
  - Results in reduction of oxygen requirements.

- Toxicity: Excessive inhibition of Ca influx can cause serious cardiac depression - bradycardia, AV block, cardiac arrest and heart failure - rare in clinical use.