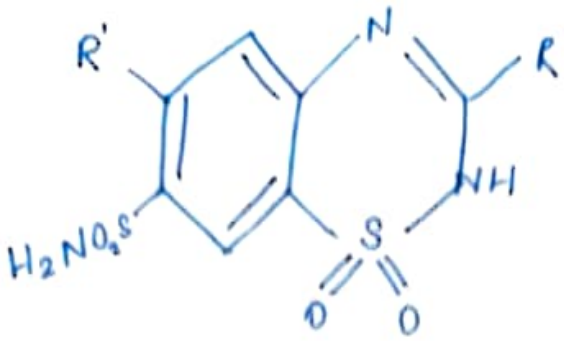
✡ SAR of Thiazides



- Sulphamoyl group → Essential for activity
- Substitution of activating group [Cl, Br & CF_3 group) at R' position → Essential for activity.
- Saturation of double bond b/w 3rd - 4th position → ↑diuretic activity 3-10 fold
- Substituent ε hydrophobic characters at R position → eg. Hydrochlorthiazide ↑s saluretic activity 1000 times
- 2nd position can tolerate small alkyl group (eg. $[CH_3]$)
- At 2nd position, Hydrogen is more acidic → due to the presence of neighbouring "Sulphone group" [ε⁻ withdrawing grp]
- Substitution of ethyl group at the position of 4, 5 & 8 → loss of diuretic activity.