

# ANTHMANIC DRUGS (Mood Elevator or Stabilizers)

Dr. Kamlesh P. Patel

Associate Professor

Department of Pharmacology

Smt. NHL Municipal Medical College

Ellisbridge, Ahmedabad.

Antimanic drugs -Dr. Kamlesh Patel- Pharmacology -  
NHLMMC

# Lithium Carbonate

- Is a monovalent cation
- First introduced in 1949 for Treatment of Mania
- Also known as ‘Antimanic’ or ‘Mood Stabilizer’
- Prevents mood swings in patients of Bipolar affective disorders (Manic Depressive Psychosis-- MDP)
- Other drugs used are :- Verapamil (Ca- channel Blockers) & Anti-epileptic drugs like Carbamazepine, Lamotrigine, Sodium valproate & Clonazepam:- GABA– mimetic anticonvulsants.

# Lithium Carbonate- MOAs

## —1) Effect on Ion Transport :-

- Li<sup>+</sup> partly replaces body Na<sup>+</sup> & is equally distributed in & outside the cell.
- Affects ionic fluxes across the brain cell or modify the property of cell membrane.
- Hence, affect generation of action potential

# Lithium Carbonate- MOAs

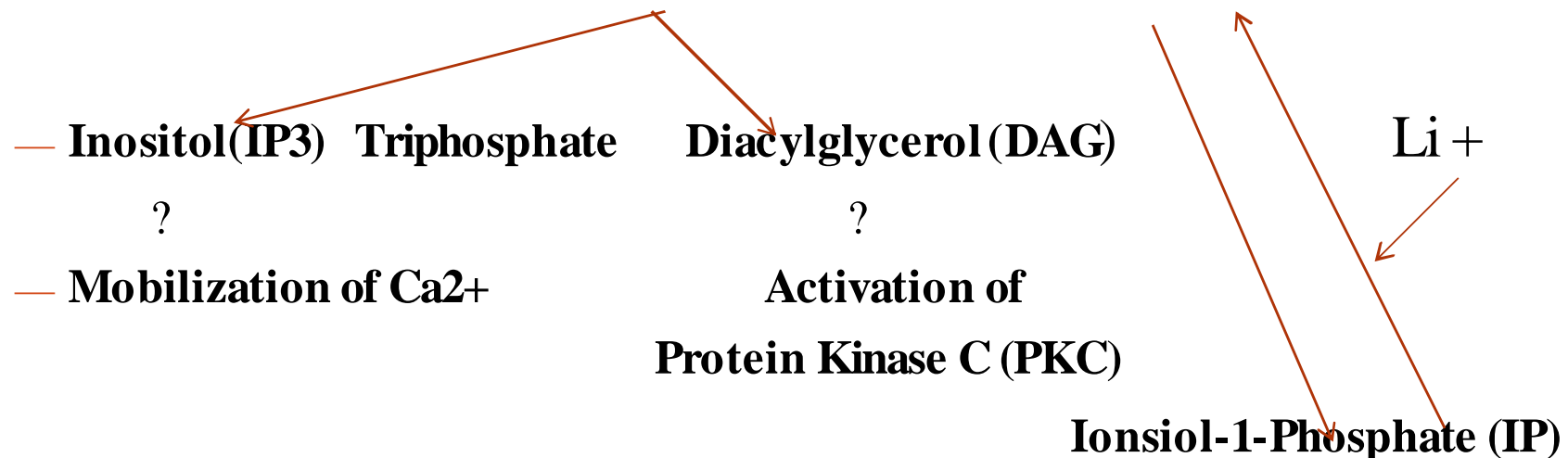
- 2) Effect on Brain Neurotransmitters :-
- Decreases release of NA & DA.
- Correct the imbalance of neurotransmitters in brain

# Lithium Carbonate- MOAs

- 3) Effect on second messengers(IP3 & DAG) ÷
- Li<sup>+</sup> inhibits the hydrolysis of inositol-1-phosphate
- Depletion of source of second messenger PIP2 (Phosphatidylinositol-4,5,biphosphate)
- Reduced release of IP3 & DAG
- Decreased activation of protein kinase C & decreased ionization of intracellular Ca<sup>2+</sup>
- Modification of neurotransmitter release & neuronal discharge (At pl. Conc of 1m mol/ L)
- Hyperactive neurones involved in manic states are affected due to limited supply of inositol from extracellular source.
- Thus, Li<sup>+</sup> dampens signal transduction in overactive neurones in mania.

# Lithium Carbonate–Distribution

- Widely distributed in total body water
- Equal distribution in both intracellular & extracellular compartments
- **Phosphatidyl inositol 4,5, bisphosphonates (PIP2)**



# Lithium Carbonate- Pharmacokinetics

- Absorption** :- Complete intestinal absorption in 6-8 hrs.
- Peak Plasma Concentration** :- ½ to 2 hrs.
- Metabolism** :- None
- Excretion** :- Urinary excretion.
- Plasma Half-Life** :- 20 hrs.

# Lithium Carbonate— Therapeutic Uses

- 1) Acute Manic Episode :-** Effective but slow response. Initially, control acute symptoms by I.M. Neuroleptics with or without Diazepam, and then add  $\text{Li}^+$  after 5-7 days. Then gradually withdraw neuroleptics.
- Maintain Plasma Conc of  $\text{Li}^+$  between 0.75 to 1.25 mEq/ Litre.
- 2) Prophylaxis of manic depressive illness :-**
- Pl. Conc of  $\text{Li}^+$  between 0.5 -1.0 m Eq/ L à Lengthens the interval between the cycles of mood swings
- Episodes of both mania & depression are attenuated.



# Lithium Carbonate— Therapeutic Uses

- 3) Depression :-** Li with other antidepressants as an add-on drug in the treatment of severe recurrent depression.
- 4) Cancer chemotherapy :-** Li<sup>+</sup> increases Leukocyte count and is used in leukopenia following cancer chemotherapy.
- 5) Other Uses :-** recurrent neuropsychiatric disorders, childhood mood disorders, hyperthyroidism & inappropriate ADH secretion syndrome.

# Lithium Carbonate— Adverse Effects

- Potentially Toxic with low Therapeutic Index
- Toxicity directly related to its Plasma concentration
- Prophylactic Pl. Conc :- 0.5 -1.0 m Eq/ L
- Therapeutic Pl. Conc. :- 0.75 – 1.25 mEq/ L
- Fatal Conc. :- 3 – 5 mEQ/ L
- **1) Mild Toxicity ( at Pk. Pl. Conc.) :-**
- N, V, abdominal pain, diarrhoea & fine tremors

# Lithium Carbonate— Adverse Effects

## —2) Acute Intoxication :-

- Vomiting, profuse diarrhoea, coarse tremors, ataxia, blurred vision, nystagmus & weight gain.
- Mental confusion, hyperpyrexia, convulsions, muscles twitchings, coma & death.
- Cardiac arrhythmias, hypotension, albuminuria and renal failure.

# Lithium Carbonate– Adverse Effects

## —3) Other side effects :-

- Benign, diffuse & non-tender enlargement of thyroid gland due to increased TSH secretion.
- Acquired nephrogenic diabetes insipidus – manifested as polydipsia, polyuria – may appear early in the treatment & then disappear. In late developing polyuria, evaluate the renal function, lower the dose of  $\text{Li}^+$  or consider addition of Thiazide or amiloride.

# Lithium Carbonate– Adverse Effects

- If administered during pregnancy – neonatal goitre, cardiovascular anomalies may occur.
- DRUG INTERACTIONS:**
- NSAIDs decrease Lithium elimination & enhance toxicity.
- Interaction with Loop diuretics – Increases toxicity of  $\text{Li}^+$ .

# Lithium Carbonate– Precautions

- 1) Minimum effective dose should be used.
- 2) Patients should always use the same formulations.
- 3) Patients should be made aware of the first symptom of toxicity.
- Li<sup>+</sup> is contraindicated in pregnancy.