A Comparative Pharmacological Study of Diuretic Drugs

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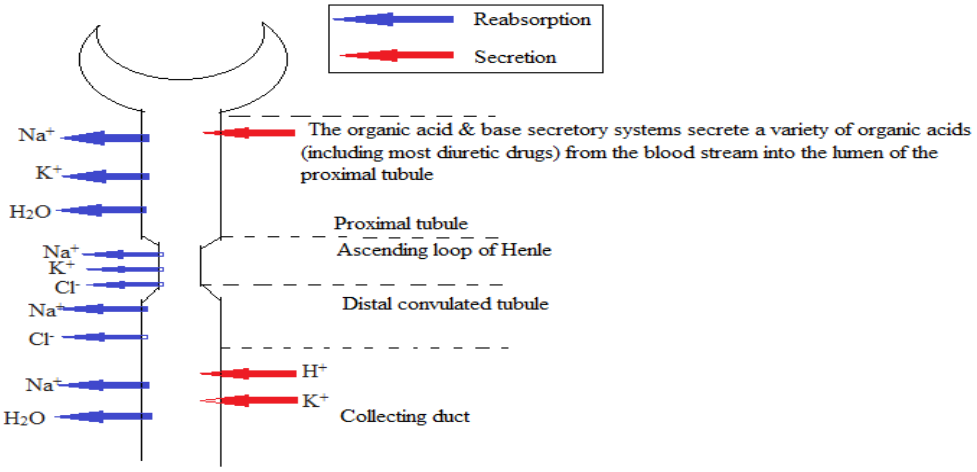
ABSTRACT

Diuretic are the drugs that promote the output of urine excreted by kidney. The increased excretion of water & electrolytes by the kidney is dependent on 3 different process viz. glomerular filtration, tubular reabsorption & tubular secretion. Diuretic are very effective in the treatment of cardiac oedema, specifically the one related with congestive heart failure(C.H.F). They are extensively used in various type of disorders for ex. Cirrhosis of liver, Hypertension,Nephritic syndrome, diabetes insipidus, nutritional oedema, oedema of pregnancy & also to lower intraocular & cerebrospinal fluid pressure. The presented article is based on comprehensive idea about the pharmacology of various diuretic drugs.

Keywords: Nephron, C.H.F, Edema, PCT,DCT

INTRODUCTION



(Nephron : Physiology of urine formation)

All soluble constituents of blood minus the plasma proteins and lipids are filtered at the glomerulus. More than 99% of the glomerular filtrate is reabsorbed in the tubules, about 1.5L urine is produced in 24 hours.

Three different processes that involve in urine formation are glomerular filtration (180L/day), tubular re-absorption (around 98%) & tubular secretion. Reabsorption occur in Proximal convoluted tubule, thick portion of ascending limb of the loop of Henle, distal convoluted tubule & in cortical collecting tubule is 60-70%, 25%, 5-10%, 5% respectively.

The purpose of using diuretics is to maintain urine volume (e.g.: renal failure) ,to mobilize edema fluid (e.g.: heart failure,liver failure, nephrotic syndrome), to control high blood pressure. Potency of a diuretic is related to the absolute amount of drug (e.g mg/Kg) required to produce an effect. While efficacy relates to the maximum diuretic effect (usually measured in terms of urine volume/time or urine loss of Na^+ or NaCl/time). Diuretics may be broadly classified under the following two categories.

(a) Mercurial diuretics: It contains Hg^{2+}. These are not very much used in clinical practices due to their pronounced and marked side-effects *viz.,* mercurialism, hypersensitivity and excessive diuresis which may lead to electrolyte depletion and vascular complications. Most of the mercurials are administered by intramuscular route and the availability of orally active diuretics has limited their use. Diuretics come under this are Chlormerodrin Hg 197, Meralluride, Mersalyl and Mercumatilin sodium etc.

(b) Non-mercurial diuretics: It is having wider applications due to fewer side-effects[1].

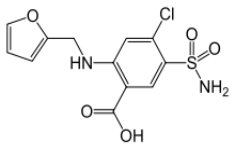
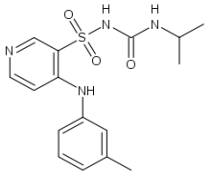
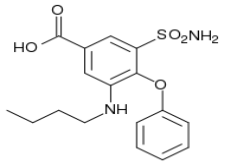
It may be classified into following type:

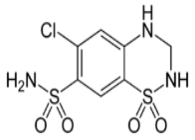
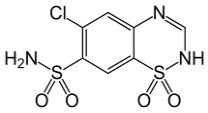
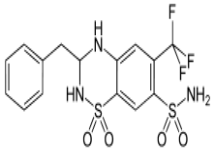
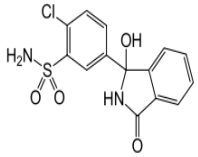
1. Thiazides (Benzothiadiazines),
2. Carbonic-Anhydrase Inhibitors,
3. Miscellaneous Sulphonamide Diuretics,
4. Aldosterone Inhibitors,
5. 'Loop' or 'High-Ceiling' Diuretics,
6. Purine or Xanthine Derivatives,
7. Pyrimidine Diuretics,
8. Osmotic Diuretics,
9. Acidotic Diuretics and
10. Miscellaneous Diuretics.

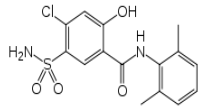
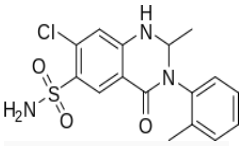
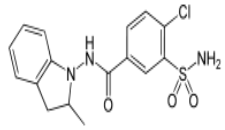
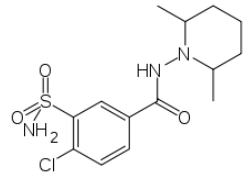
Diuretics are acting at different sites in the nephron. Carbonic anhydrase inhibitors acting at the proximal convoluted tubule (site1 diuretics). Loop diuretics acting at the Henle's loop (site 2 diuretics). Thiazides and thiazide-like diuretics acting at distal convoluted tubule (site 3 diuretics). Potassium-sparing diuretics acting at collecting tubule(site 4 diuretics). Osmotic diuretics act at proximal tubules, loop of henle, collecting tubule. According to type of electrolyte excreted it may be named as follows:

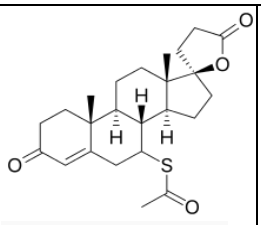
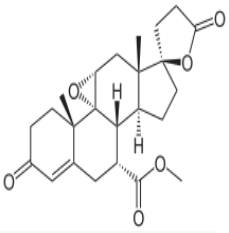
Chloruretic	Cl^-
Natriuretic	Na^+
Saluretic	Nacl
Kaliuretic	K^+
Bicarbonaturetic	HCO_3^-

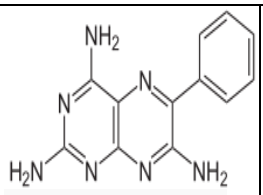
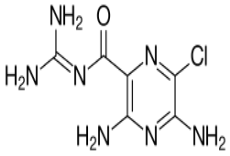
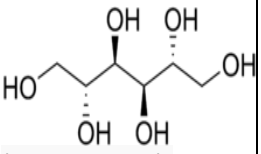
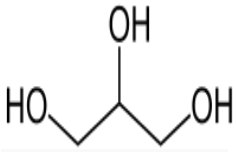
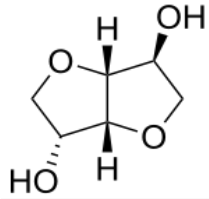
Some of the diuretic drugs with their pharmacological action are tabulated as below:

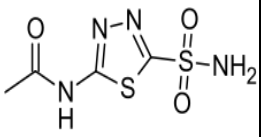
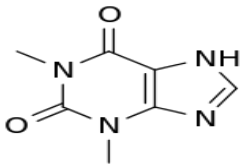
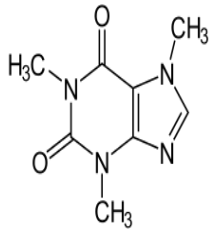
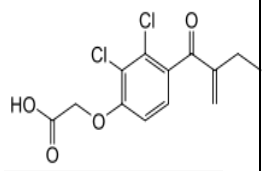
S.N	Drug	Mechanism Of Action	Pharmacokinetic	Adverse Effect	Clinical Uses	Reference
1	FURESEMIDE  4-chloro-2-[(furan-2 ylmethyl)amino]- 5-sulfamoylbenzoic acid	Inhibit Na^+-k^+-$2Cl^-$ co-transporter of ascending loop of henle	Administer orally, IV& IM , Plasma $t_{½}$ is 1- 2 hours, Low lipid solubility, Protein binding 91–99%,	Hypokalaemia , Metabolic alkalosis, Hypovolaemia, Hyperuricaemia, Allergy Excreted unchanged in urine 80–90 %, Volume of distribution (L/kg) 0.07–0.2%	Used in pulmonary & cerebral Oedema, Hypertension, Hypercalcaemia of malignancy	Tripathy et al[2]
2	TORASEMIDE  N[(isopropylamino) carbonyl]-4-[(3-methylphenyl)amin o]pyridine-3-sulfonamide	Inhibit Na^+-k^+-$2Cl^-$ co-transporter of ascending loop of henle	Administer orally, IV, plasma $t_{½}$ -3.5 hours ,dose(2.5-5mg in hypertension, 5-20mg in oedema	Hypokalaemia, Metabolic alkalosis, Hypovolaemia, Hyperuricaemia, Allergy	Mainly used in the management of edema associated with C.H.F , used at low doses for the management of hypertension	Dunn CJ et al [3]
3	BUMETAMIDE  butylamino-4-phenoxy-5-sulfamoyl-benzoic acid	Inhibit the Na^+-k^+-$2Cl^-$ co-transporter of ascending loop of henle.	Use orally,IV&IM , Plasma t ½ -1 hours, Bioavailability- 80 to 100%	Hypokalaemia, Metabolic Alkalosis, Hypovolaemia, Hyperuricaemia, Allergy	Pulmonary & cerebral Oedema, Hypertension, Hypercalcaemia of malignancy	Rang et al[4]

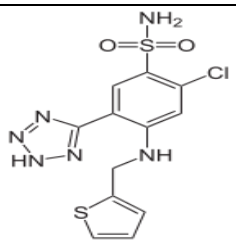
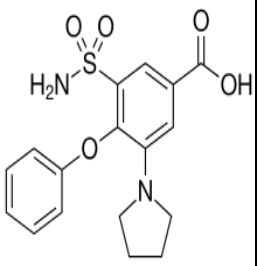
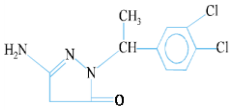
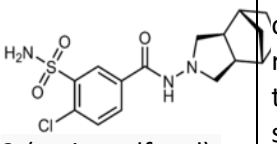
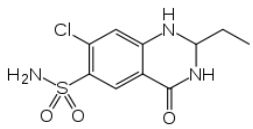
4	HYDROCHLOROTHAIZIDE  6-chloro-1,1-dioxo-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulfonamide	Inhibit Na^+-$2Cl^-$ symporter in DCT(site -3)	Use orally, bioaviability-70%, On set of action-4-6 hours, Duration of action-8-12 hours, Excreted 95% unchanged in urine.	Hypokalemia, Hyperuricemia, Hyperglycemia Hyperlipidemia, Headache, Nausea/ vomiting, Photosensitivity, Weight gain, Gout, Pancreatitis	Hypertension, Congestive Heart Failure, Symptomatic edema, Diabetes, Insipidus, Renal Tubular Acidosis.	R.A Harvey et al[5]
5	CHLOROTHAIZIDE  (*RS*)-2-Chloro-5-(1-hydroxy-3-oxo-2,3-dihydro-1*H*-isoindol-1-yl)benzene-1-sulfonamide	Inhibit Na^+-$2Cl^-$ symporter in DCT(site -3)	Absorbed orally, Action starts within 1 hour, but the duration varies from 8–48 hours	Nausea ,Vomiting, Headache, Dizziness, Excess urine production, Dehydration, Hypoelectrolytemia	Used to treat Edema in people with C.H.F, Cirrhosis of liver, Kidney disorders or edema caused by taking steroids or oestrogen, Used to treat hypertension	Tripathy et al[2]
6	BENDROFLUMETHIAZIDE  Benzyl-1,1-dioxo-6-(trifluoromethyl)-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulfonamide	Inhibit sodium reabsorption at the beginning of the DCT.	Oral use, Adverse interaction with alcohol, not be used by pregnant women	Common adverse effects: Postural Hypotension, hyponatraemia, Hypokalaemia, Hypercalcaemia,Gout, Impaired glucose tolerance, impotence, fatigue, Pulmonary Oedema, Pneumonitis Rare adverse effects: Thrombocytopenia, Agranulocytosis, Photosensitivity, Rash, Pancreatitis, Renal Insufficiency	Used for the treatment of mild heart failure, hypertension	Satoskar et al[6]
7	CHLORTHALIDONE  (*RS*)-2-Chloro-5-(1-hydroxy-3-oxo-2,3-dihydro-1*H*-isoindol-1-yl)benzene-1-sulfonamide	Inhibit Na^+-Cl^- symporter in DCT	Oral use,dose-50-100mg/day, Duration of action is48 hours, Excreted unchanged in urine, t½ 40–50 hours	Hypokalemia, Hypochloremia, mild metabolic alkalosis.	Used exclusively as antihypertensive.	Tripathy et al[2]

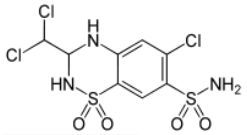
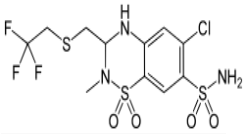
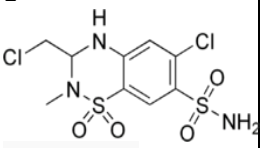
8	XIPAMIDE  4-chloro-*N*-(2,6-dimethylphenyl)-2-hydroxy-5-sulfamoy-lbenzamide	Acts on kidney to reduce sodium reabsorption in DCT	After oral administration 20 mg are reabsorbed quickly & reach the plasma conc. Of 3 mg/l with in 1hr. Diuretic effect starts after 1 hr of administration & lasts for nearly 24 hr. Plasma clearance is 30-40 ml/min.	Hypokalaemia, Hyponatraemia, Thrombocytopenia, Leucopenia, Acute interstitial nephritis Hyperlipidemia, Orthostatic hypotension	Used for cardiac edema caused by decompensation of heart failure, Renal edema, chronic renal disease, Hepatic edema caused by cirrhosis ascites lymphoedema, Hypertension	Jasek et al[7], Klopp et al [8]
9	METALAZONE  7-chloro-2-methyl-4-oxo-3-o-tolyl-1,2,3,4-tetrahydroquinazoline-6-sulfonamide	Inhibit sodium-chloride symporter	Oral use, Excreted unchanged in urine, Duration of action 12-24 hours	Aplastic anaemia, Pancreatitis, Agranulocytosis, Angioedema, Abnormalities of water balance, electrolyte levels.	Used mainly for edema (5–10 mg/day, rarely 20 mg), and occasionally for hypertension (2.5–5 mg/day).	Tripathy et al [2]
10	INDAPAMIDE  4-chloro-N-(2-methyl-2,3-dihydroindol-1-yl)-3-sulfamoyl-benzamide	Inhibit Na^+-Cl^- symporter in DCT	Oral use, highly lipid soluble,dose-2.5-5mg/day, duration of action-12-24 hours	Hypokalemia, Fatigue, Orthostatic hypotension, Allergic menifestations	Hypertension, Decompensated hypertension.	Tripathy et al[2]
11	CLOPAMIDE  4-chloro-*N*-(2,6-dimethyl-1-piperidyl)-3-sulfamoyl-benzamide	It act in kidney at PCT of nephron where it Na^+-Cl^- symporter	Oral absorption 100 %, Plasma protein binding is < 50%, Plasma half life is 10 hr.	Hypokalemia, hyperglycemia Nausea, Vomiting, Diarrhoea, Loss of appetite, Blurred vision, Dizziness.	Used in hypertension , Edema associated with heart failure	Tripathy et al[2]
12	SPIRONOLACTONE	It is a competitive antagonist to the	The oral bioavailability from microfine powder tablet is	Drowsiness, Ataxia, Mental confusion, Epigastric distress	Edema, Hypertension, C.H.F, It is a weak diuretic	Tripathy et al[2]

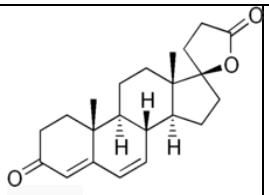
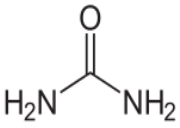
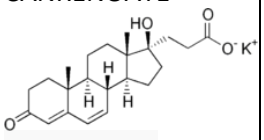
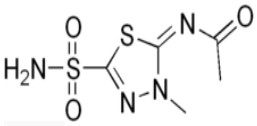
	 7α-Acetylthio-17α-hydroxy-3-oxopregn-4-ene-21-carboxylic acid γ-lactone	mineralocorticoids such as aldosterone. The mineralocorticoid receptor is an intracellular protein in nature that can bind aldosterone. Spironolactone binds to the receptor and competitively inhibits aldosterone binding the the receptor. The inability of aldosterone to bind to its receptor prevents reabsorption of Na+& Cl-and associated water.	75%, It is highly bound to plasma proteins, Completely metabolized in liver, The most important active metabolite is Canrenone. The t½ of spironolactone is 1–2 hours, while that canrenone is ~18 hours.	and loose motions.	and is used only in combination with other more efficacious diuretics.	
13	EPLERENONE  pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo, γ-lactone, methyl ester (7α, 11α, 17α)	It is an antagonist of the mineralocorteccoid receptor.	well absorbed orally, t½ is 4–6 hours, Plasma protein binding is 50 %, Oral bioavailability is 69% following administration of 100 mg oral tablet, Metabolism is mediated via CYP3A4,	Hyperkalemia, Hypotension, Dizziness, Altered renal function, Increased creatinine concentration.	Used in moderate to severe CHF, Post-infarction left ventricular dysfunction, Hypertension, can be used as alternative to spironolactone.	Rossi et al[9]
14	TRIAMTERENE	It acts by blocking the epithelial sodium channel on the lumen	It is incompletely absorbed orally, partly bound to plasma proteins, largely	Nausea, Dizziness, Muscle cramps, Rise in blood urea. Impaired glucose	Hypertension, Edema	Tripathy et al[2]

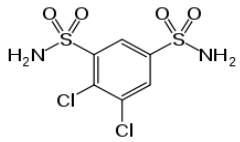
	 6-phenylpteridine-2,4,7-triamine	side of the kidney collecting tubule.	metabolized in liver to an active metabolite and excreted in urine. Plasma t½ is 4 hours, effect of a single dose lasts 6–8 hours.	tolerance and photosensitivity		
15	AMILORIDE  3,5-diamino-6-chloro-*N*-(diaminomethylene)pyrazine-2-carboxamide	Act by directly blocking the epithelial sodium channel in the late DCT in the kidney	Only ¼ of an oral dose is absorbed, It is not bound to plasma proteins and not metabolized, The t½ (20 hours) and duration of action are longer than triamterene.	Nausea, Headache, Diarrhoea.	Hypertension, C.H.F, Cystic fibrosis.	Tripathy et al[2]
16	MANNITOL  (2*R*,3*R*,4*R*,5*R*)-Hexane-1,2,3,4,5,6-hexol	It is act on the proximal tubules & inhibit both water & solute reabsorption in the kidney tubule by increasing the osmolarity of the renal tubular fluid.	It is not absorbed orally, Has to be given i.v. as 10–20% solution, It is excreted with a t½ of 0.5–1.5 hour.	Pulmonary congestion, Fluid & electrolyte imbalance, Dryness of mouth, Thrist, Edema, Urinary retention, Headache, Blurred vision	Used in acute congestive heart, Glaucoma, Head injury, Shock , Severe trauma, Cardiac surgery	Satoskar et al[6]
17	GLYCEROL  propane-1,2,3-triol	It acts by expanding extracellular fluid & plasma volume, therefore increasing blood flow to the kidney	Orally active osmotic diuretics, Dose: 0.5–1.5 g/kg as oral solution	Intravenous glycerol can cause haemolysis.	Used to reduce intraocular or intracranial tension	Satoskar et al[6]
18	ISOSORBIDE  1,4:3,6-Dianhydro-D-sorbitol; 1,4-	No direct effect on transport but cause shift of ions by inducing bulk water flow & changing steady state water concentration	Orally active osmotic Diuretics, Dose: 0.5–1.5 g/kg as oral solution	Hypotension, Hypovolemia, Heart failure, Pulmonary congestion, Headache, blurred vision, Nausea, vomitting	Used to reduce intraocular or intracranial tension	Tripathy et al[2]

	Dianhydrosorbitol	in body compartment.				
19	ACETAZOLAMIDE  N-(5-sulfamoyl-1,3,4-thiadiazol-2-yl)acetamide	Inhibits CAse (type II) in PT Cells, Inhibition of CAse (type IV), The net effect is inhibition of HCO^- (and accompanying Na+) reabsorption in PT.	Well absorbed orally, Excreted unchanged in urine. Action of a single dose lasts 8–12 hours.	Acidosis, Hypokalaemia, Drowsiness, Paresthesias, Fatigue, Abdominal Discomfort. Hypersensitivity reaction, Bone marrow depression.	Glaucoma, To alkalinise urine, Epilepsy, Acute mountain sickness, Periodic paralysis	Tripathy et al[2]
20	THEOPHYLLINE  1,3-Dimethyl-7*H*-purine-2,6-dione	Mechanism unclear, may be related to inhibition of phosphodiesterase and/ or antagonism of adenosine receptor	Bioavailability is 100% in case of IV, Metabolized in liver (70%), Excreted unchanged in urine,	Nausea, diarrhoea, Abnormal heart rhythm, CNS excitation, seizure	Increasing renal blood flow, Relaxing bronchial smooth muscle, COPD.	Rieg T et al [11], Yoshikawa et al [12]
22	CAFFINE  1,3,7-Trimethylpurine-2,6-dione	Mechanism unclear, may be related to inhibition of phosphodiesterase and/ or antagonism of adenosine receptor	Metabolized in the liver, In healthy adults $t_{1/2}$ is 3-7 hr, Nicotine decrease the half life by 30-50 %	Increase metabolic rate, Anxiety, Vasoconstriction,	Relax smooth muscle of bronchi & is used to treat Asthma	Rieg T et al[11]
23	ETHACRYNIC ACID  [2,3-dichloro-4-(2-methylenebutanoyl)phenoxy]acetic acid	Inhibit the Na^+-k^+-$2Cl^-$ co transporter of ascending loop of henle (site-2)	Oral use, $t^{1/2}$-~1 hr, Metabolised ~33% in liver, Excreted in urine ~62%.	Hypokalaemia, metabolic alkalosis, Hypovolaemia , Hyperuricaemia, Allergy	Oedema like (pulmonary, cerebral), hypertension	Goodman et al[10]
24	AZOSEMIDE	It is a high ceiling diuretic. Exact mechanism is not understood But it mainly	Oral boavailability in human is aprox. 20.4%, It's effect is 5.5-8 time greater than	Panic disorder, Liver disorder, Blood creatine phosphokinase increased	Used in the treatment of oedematous states, Hypertension.	Kim et al[13]

	 2-chloro-5-(2H-tetrazol-5-yl)-4-[(thiophen-2-ylmethyl)amino]benzenesulfonamide	act on both medullary & cortical segment of thick ascending limb of the loop of henle.	furosemide. Apparent post-pseudodistribution volume is 0.0262 l/kg, In human total body clearance, renal clearance, terminal half life is 112ml/min, 41.6 ml/min, 2.03 hr respectively.			
25	PIRETANIDE  3-(aminosulfonyl)-4-phenoxy-5-pyrolidin-1-yl benzoic acid.	Site of action is thick ascending limb of the loop of henle.	Oral use , $t^{1/2}$-~0.6-1.5 hours, Metabolised ~50% in liver, Excreted in urine ~50%.	Excess loss of fluid & electrolyte.	Use for the treatment of hypertension, C.H.F & edematous state caused by renal & hepatic disease.	Goodman et al[10]
26	MUZOLIMINE  3-Amino-1-(3,4-dichloro-⟨-methylbenzyl)-2-pyrazolin-5-one	It is a loop diuretic	Effect is slow, It's action is long lasting.		Used for hypertension but was withdrawn because of severe neurological side effect.	Reyes et al[14]
27	TRIPAMIDE  3-(aminosulfonyl)-4-chloro-*N*-[(3a*R*,4*S*,7*R*,7a*S*)-octahydro-2*H*-4,7-methanoisoindol-2-yl]benzamide	Inhibitory effect on solute reabsorption at the cortical segment of thick ascending limb of loop of henle.	Oral use, Metabolised in liver	Hypokalaemia, metabolic alkalosis, Hypovolaemia , Hyperuricaemia, Allergy	Hypertension, Edema.	Goodman et al [10]
28	QUINETHAZONE 	It inhibit active chloride reabsorption at the early distal tubule via Na-Cl	Onset of action 2 hr, Duration of action 18-24 hr. Time to peak	Dizziness, Dry mouth, Nausea, Low potassium level.	Diuretic and antihypertensive properties similar to those of the thiazides.	Satoskar et al[6]

	7-chloro-2-ethyl-4-oxo-1,2,3,4-tetrahydroquinazoline-6-sulfonamide	cotransporter	effect 6 hr.			
29	TRICHLORMETHIAZIDE  6-Chloro-3-(dichloromethyl)-1,1-dioxo-3,4-dihydro-2*H*-benzo[*e*][1,2,4]thiadiazine-7-sulfonamide	Inhibit Na+/2Cl_symporter in DCT(site-3)	Oral use , $t^{1/2}$-~2.3-7.3 hours, Excreted in urine	Hypokalemia, Hyperurecaemia, Hyperlipidimia, Hyperglycemia, Hypersensitivity, Thrombocytopenia, Volume depletion, Hyponatraemia	Hypertension, Heart failure, Diabetes insipidus, Hypercalciurea	Goodman et al [10]
30	POLYTHIAZIDE  6-chloro-2-methyl-3-{[(2,2,2-trifluoroethyl)thio]methyl}-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide	Enhance urinary excretion of both Na and H2O by specifically inhibiting Na reabsorption located in the cortical (thick) portion of the ascending limb of Henle's loop and also in the early distal tubules.	Normal human subjects receiving single 1mg oral dose, the mean plasma half life for absorption & elimination were 1.2 & 25.7 hr respectively, 25 % excreted unchanged in urine.	Abdominal or stomach pain, Bleeding gum, Blurred vision, Chest pain, Blood in urine or stool.	Long-acting diuretic and anti-hypertensive agent. As diuretic, usual, 1 to 4 mg per day As antihypertensive, 2 to 4 mg	Hobbs et al[15]
31	METHYCLOTHIAZIDE  6-Chloro-3-(chloromethyl)-2-methyl-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide	Enhance urinary excretion of both Na and H_2O by specifically inhibiting Na reabsorption located in the cortical (thick) portion of the ascending limb of Henle's loop and also in the early distal tubules.	Given orally, Rapid absorption, Cross the placenta, Elimination through kidney. Duration of action 6 hr	Anxiety, Sweating, Severe shortness of breath, Cough with foamy mucus, Increased thrist, Drowsiness, Muscle pain, Fainting or seizure, Nausea, Vomiting.	Diuretic and an antihypertensive agent. 2.5 to 10 mg once per day	Asutosh et al[1]
32	CANRENONE	Inhibit binding of aldosterone	Oral use, $t^{1/2}$-~16.5 hours,	Drowsiness, Ataxia,	Oedema, hypertension, CHF	Goodman et al[10]

	 10,13-Dimethylspiro[2,8,9,11,12,14,15,16-octahydro-1*H*-cyclopenta[a]phenanthrene-17,5'-oxolane]-2',3-dione	with mineralocorticoid receptor.		Mental confusion		
33	UREA 	No direct effect on transport but cause shift of ions by inducing bulk water flow & changing steady state water concentration in body compartment.	Used intravenously, It penetrate total body water, short half life,	Hypotension, Hypovolemia, Heart failure, Pulmonary congestion, Headache, blurred vision, Nausea, vomitting	Approved to reduce intraocular pressure, intracranial pressure, Cerebral edema	Goodman et al[10]
34	POTASSIUM CANRENOATE  potassium 3-[(8*R*,9*S*,10*R*,13*S*,14*S*,17*R*)-17-hydroxy-10,13-dimethyl-3-oxo-2,8,9,11,12,14,15,16-octahydro-1*H*-cyclopenta[a]phenanthren-17-yl]propanoate	It is an aldosterone antagonist.	Given intravenously	Nausea, vomiting, Confusion, Restlessness, Hallucination.	Oedema	Goodman et al[10]
35	METAZOLAMIDE  *N*-[5-(aminosulfonyl)-3-methyl-1,3,4-thiadiazol-2(3*H*)-ylidene]acetamide	Carbonic anhydrase inhibitor	Oral use, $t^{1/2}$-~14 hours, Metabolise~75%, Renal excreation of intact drug~25%	Acidosis, drowsiness, Paresthesias , Abdominal Discomfort, Fatigue, Hypertension.	Glaucoma, Epilepsy, periodic paralysis.	Goodman et al[10]

36	DICHLORPHENAMIDE  4,5-Dichlorobenzene-1,3-disulfonamide	Carbonic anhydrase inhibitor	Oral use	Dizziness, Change in the sense of test, Headache, Confusion, Weight loss, muscle pain, joint pain, Throat pain, rash	Glaucoma, Epilepsy	Goodman et al[10]

Selected Drug- Diuretic Interaction:

DRUGS	DIURETCS	PROBLEMS
Digitalis	Loop & thiazide	Hypokalemia → digitalis toxicity
NSAID	Loop & thiazide	Decrease diuretic effect
Aminoglycoside	loop	Ototoxicity & nephrotoxicity
Adrenal steroids	Loop & thiazide	Severe hypokalemia
Chlorpropamide	Thiazide	Hyponatremia
Lithium	Loop & thiazide	Increased plasma (lithium)
Probenecid	Loop & thiazide	Decrease diuretic effect
ACE inhibitors	K+ sparing	Hyperkalemia → Arrhythmias

CONCLUSION

By increasing the urine flow rate diuretic usage leads to increase excretion of electrolytes (especially Na^+ & Cl^-) and water from the body without affecting protein, vitamins, glucose amino acids reabsorption & capable of solving various type of diseases mention above.

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