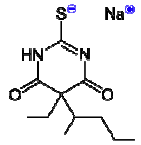
CODE- AS 2531

B. Pharam. VII SEMESTER EXAMINATION, 2013

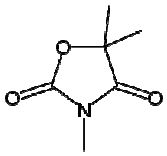
Pharmaceutical Chemistry VII (Medicinal Chem -III)

SECTION- A

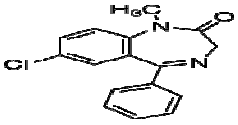
i) Structure of Thiopental sodium .



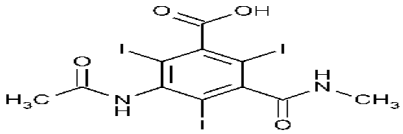
ii) Structure of Trimethadione.



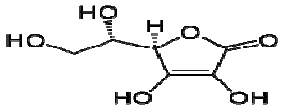
iii) Structure of Diazepam.



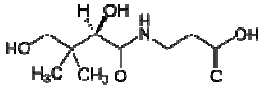
iv) Structure of Iothalamic acid.



v) Structure of Vitamin –c.



vi) Structure of Pantothenic acid.



Q1. b) IUPAC name of indomethacin .

is 1-(p chlorobenzoyl)-2-methyl-6-methoxy-3-indoleacetic acid.

Q1. c) Two name of MAO inhibitors are Tranylcypromine and phenelzine.

Q1. d) The name of one diabenzodiazepine derivative drug is Clozapine

Q1. e) Applications of the .

i) Ketamine. – As anesthetics and analgesics.

ii) Diagonostic agents - for determination of blood volume and thyroid function.

iii) Codeine.- as expectorant and analgesics.

Section –B

(Descriptive questions. Each question carries 14 marks) 14 X 04 = 56

Q2. Define the term sedatives and hypnotics, Classify them. Write the structure, nomenclature and synthesis of allobarbitone, and hexobarbitone.

Answer:

sedatives refers to a queting effect accompanied by relaxation and rest but not sleep and hypnotic drugs are used to produce drowsiness and help the onset and maintenance of sleep.

Classes of sedatives and hypnotics are:-

A) Barbiturates

- amobarbital (Amytal)
- pentobarbital (Nembutal)
- secobarbital (Seconal)
- phenobarbital (Luminal)

- Benzodiazepines (trade names)
  - clonazepam (Klonopin N.America; Rivotril Europe, Asia)
  - diazepam (Valium)
  - estazolam (Prosom)
  - flunitrazepam (Rohypnol)
  - lorazepam (Ativan)
  - midazolam (Versed)
  - nitrazepam (Mogadon)
  - oxazepam (Serax)
  - triazolam (Halcion)
  - temazepam (Restoril, Normison, Planum, Tenox, and Temaze)
  - chlordiazepoxide (Librium)
  - alprazolam (Xanax)

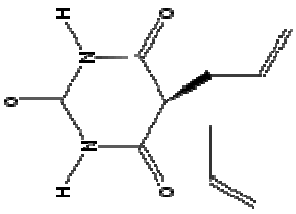
- Nonbenzodiazepine "Z-drugs" sedatives
  - eszopiclone (Lunesta)
  - zaleplon (Sonata)
  - zolpidem (Ambien)
  - zopiclone (Imovane, Zimovane)

- Antihistamines
  - diphenhydramine
  - dimenhydrinate
  - doxylamine
  - mirtazapine
  - promethazine

- Herbal sedatives

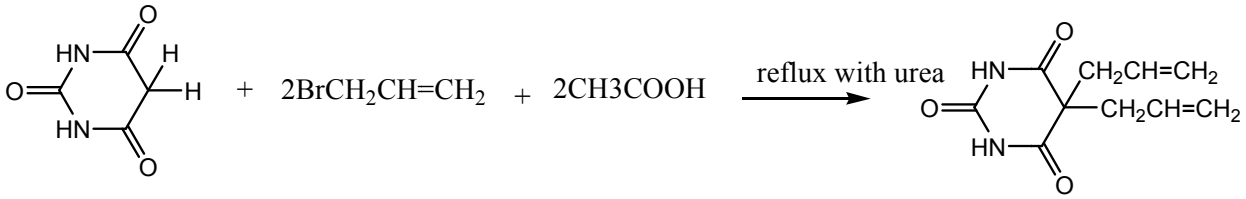
- Duboisia hopwoodii
- Chamomile
- Prostanthera striatiflora
- catnip
- kava (Piper methysticum)
- valerian
- cannabis
- passiflora spp.(passiflora incarnata)
- Validol

Allobarbitone,
Structure :-

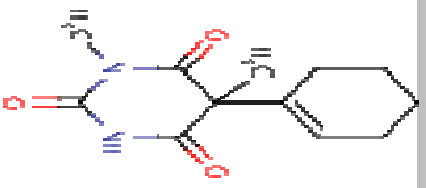


IUPAC Name: 5,5-diprop-2-enyl-1,3-diazinane-2,4,6-trione

Synthesis:

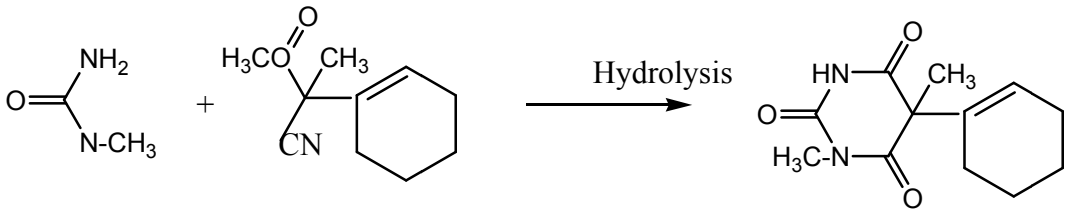


Hexobarbitone.



IUPAC Name: 5-(1-cyclohexen-1-yl)-1,5-dimethylbarbituric acid

Synthesis:



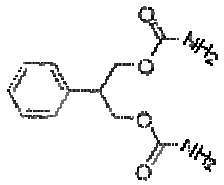
Q3. What do you understand by convulsions, classify the anticonvulsant drugs. Write the structure, nomenclature and synthesis of felbamate, gabapentin and lamotrigine .

Ans: The epilepsies or convulsions are a group of disorders characterized by chronic, recurrent, paroxymal changes in neurologic function caused by abnormalities in electrical activity of the brain.

Classes of the anticonvulsant drugs are

1)Hydantoin derivatives : Phenytoin, Ethantoin.
2)Barbiturate: Phenobarbitone,
3)Oxazolidinedione: Trimethadione, Paramethadione.
4)Succimide derivatives: Phensuccimide, ethosuccimide.
5)Miscellaneous: Gabapentin, felbamate, valproic acid and lamotrigine

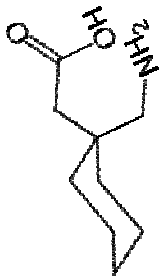
Felbamate:-



(3-carbamoyloxy-2-phenylpropyl) carbamate

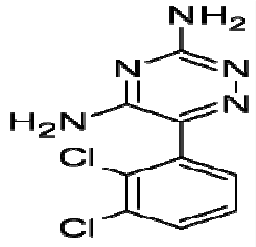
Gabapentin:

Structure:

Nomenclature:  2-[1-(aminomethyl)cyclohexyl]acetic acid

Synthesis: Cyclohexane 1,1 diacetic acid is esterified with methanol and reacted with ethyl chloroformate to yield 1-isocynatomethyl derivative of monoester. This compound is converted to the 1-(aminoethyl) product and the lactam, through the cyclization of the ester and the free amine .The mixture is refluxed with dilute HCl to give Gabapentin.

Lamotrigine:



6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine

Synthesis:-

Reaction of 2,3dichlorobenzoyl chloride with cynide ion form the benzoylcynide derivative that is then treated with aminoguanidine to form Schiff base through loss of water between the carbonyl group and primary amine function of guanidine.Ring closure by addition of the lone free amino group,remaining on the guanidine moiety to the nitrile function is accomplished by base catalysis and yield the product.

Q4.What are Neuroleptics. Enumerate the various phenothiazine derivatives. Write the structure, nomenclature and synthesis of droperidol and acetophenazine.

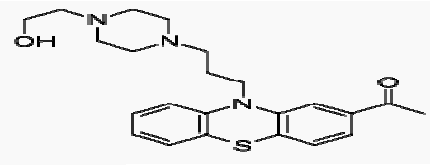
Ans: Drugs which use for management and treatment of psychosis and neuroses called neuroleptics.

Phenothiazine derivatives are given in the table

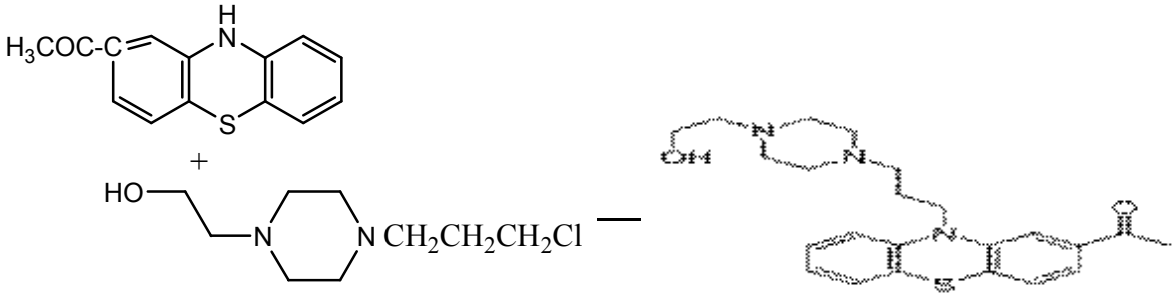
Group	Example	Sedative
Aliphatic compounds	Chlorpromazine (marketed as Thorazine, Chlor-PZ, Klorazine, Promachlor, Promapar, Sonazine, Chlorprom, Chlor-Promanyl, Largactil)	strong
	Promazine (trade name Sparine)	moderate
	Triflupromazine (trade names Clinazine, Novaflurazine, Pentazine, Terfluzine, Triflurin, Vesprin)	strong
	Levomepromazine in Germany andmethotrimeprazine in America (trade names Nozinan, Levoprome)	extremely strong
Piperidines	Mesoridazine (trade name Serentil)	strong

	Thioridazine (trade names Mellaril, Novoridazine, Thioril)	strong
Piperazines	Fluphenazine (trade names Prolixin, Permitil, Modecate, Moditen)	weak/moderate
	Perphenazine (sold as Trilafon, Etrafon, Triavil, Phenazine)	weak/moderate
	Prochlorperazine (trade names Compazine, Stemetil)	
	Trifluoperazine (trade name Stelazine)	moderate

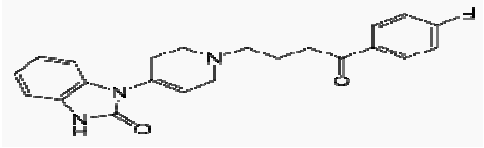
Acetophenazine



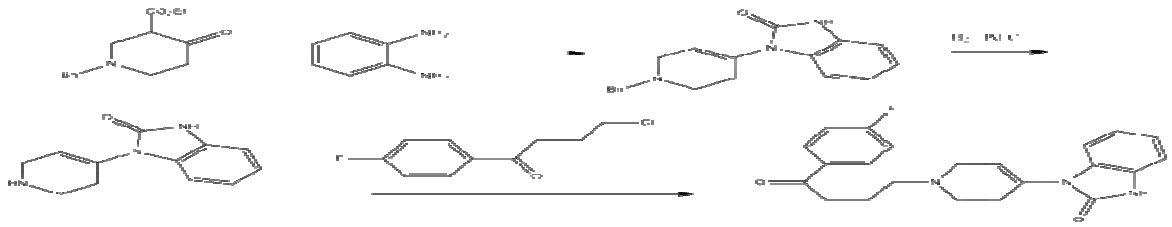
1-[10-[3-[4-(2-hydroxyethyl)piperazin-1-yl]propyl]-10H-phenothiazin-2-yl]ethanone



Droperidol



1-{1-[4-(4-fluorophenyl)-4-oxobutyl]-1,2,5,6-tetrahydropyridin-4-yl]-1,3-dihydro-2*H*-benzimidazol-2-one



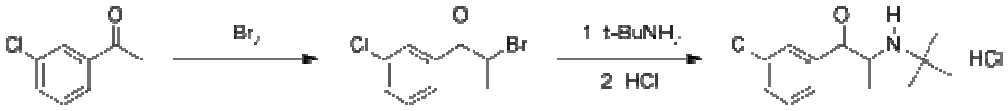
Q5. Write the classes of antidepressant drugs. Give structure, nomenclature and synthesis of bupropion, despiramine and doxepin.

Antidepressants are drugs used for the treatment of major depressive disorder and other conditions, including dysthymia, anxiety disorders, obsessive compulsive disorder, eating disorders, chronic pain, neuropathic pain and, in some cases, dysmenorrhoea, snoring, migraines, attention-deficit hyperactivity disorder (ADHD), substance abuse and sleep disorders. They can be used alone or in combination with other medications.

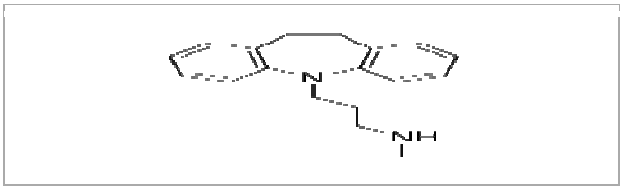
The most important classes of antidepressants are the selective serotonin reuptake inhibitors (SSRIs), serotonin–norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs). Other drugs used or proposed for the treatment of depression include buprenorphine, tryptophan, low-dose antipsychotics, and St John's wort

Bupropion:

±)-2-(*tert*-Butylamino)-1-(3-chlorophenyl)propan-1-one

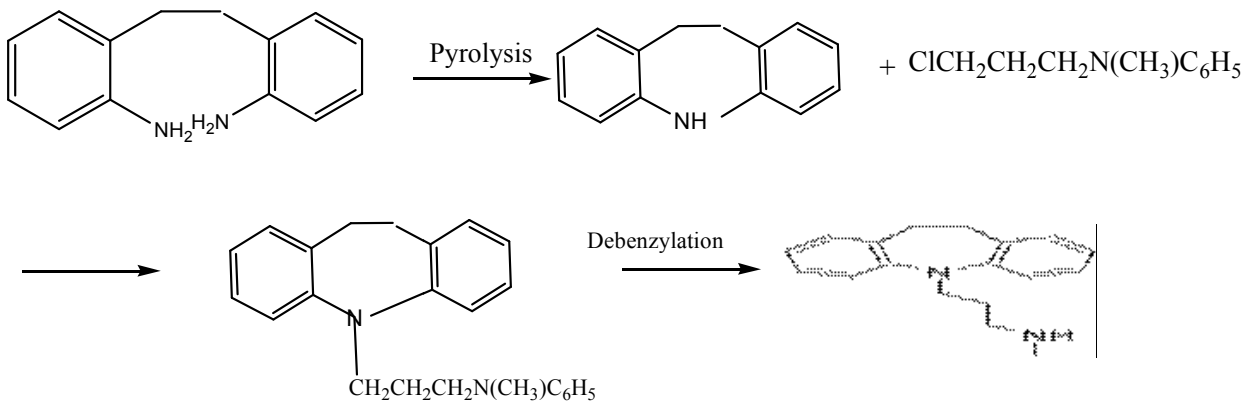


Despiramine

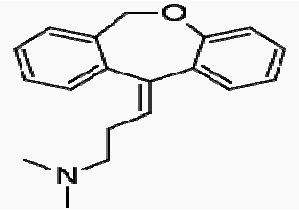


3-(10,11-dihydro-5*H*-dibenzo[*b*,*f*]azepin-5-yl)-*N*-methylpropan-1-amine

Synthesis:

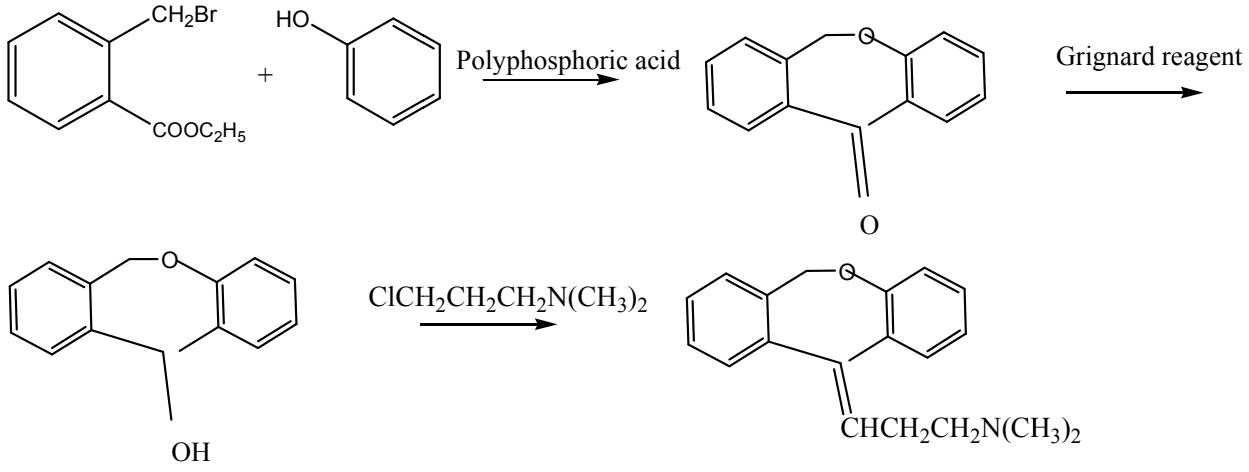


Doxepin.



Name: -3-(dibenzo[*b,e*]oxepin-11(6*H*)-ylidene)-*N,N*-dimethylpropan-1-amin

Synthesis:



Q6. Define radiopharmaceuticals. Write Pharmaceutical applications of Au, I and Co. radioisotopes.

Ans: Many of the chemical elements have a number of isotopes. The isotopes of an element have the same number of protons in their atoms (atomic number) but different masses due to different numbers of neutrons. In an atom in the neutral state, the number of external electrons also equals the atomic number. These electrons determine the chemistry of the atom. The atomic mass is the

sum of the protons and neutrons. There are 82 stable elements and about 275 stable isotopes of these elements.
When a combination of neutrons and protons, which does not already exist in nature, is produced artificially, the atom will be unstable and is called a radioactive isotope or radioisotope. There are also a number of unstable natural isotopes arising from the decay of primordial uranium and thorium. Overall there are some 1800 radioisotopes.
Radiopharmaceutical is a preparation intended for in vivo use, that contains radionuclide and use for diagnostic and therapeutic purpose.
At present there are up to 200 radioisotopes used on a regular basis, and most must be produced artificially.
Radioisotopes can be manufactured in several ways. The most common is by neutron activation in a nuclear reactor. This involves the capture of a neutron by the nucleus of an atom resulting in an excess of neutrons (neutron rich).
Some radioisotopes are manufactured in a cyclotron in which protons are introduced to the nucleus resulting in a deficiency of neutrons (proton rich).
The nucleus of a radioisotope usually becomes stable by emitting an alpha and/or beta particle. These particles may be accompanied by the emission of energy in the form of electromagnetic radiation known as gamma rays. This process is known as radioactive decay.
Radioisotopes have very useful properties: radioactive emissions are easily detected and can be tracked until they disappear leaving no trace. Alpha, beta and gamma radiation, like x-rays, can penetrate seemingly solid objects, but are gradually absorbed by them. The extent of penetration depends upon several factors including the energy of the radiation, the mass of the particle and the density of the solid. These properties lead to many applications for radioisotopes in the scientific, medical, forensic and industrial fields

Carbon-14: Used to measure the age of water (up to 50,000 years)
Chlorine-36: Used to measure sources of chloride and the age of water (up to 2 million years)
Lead-210: Used to date layers of sand and soil up to 80 years
Tritium (H-3): Used to measure 'young' groundwater (up to 30 years)

Artificially-produced radioisotopes:

Americium-241:
Used in backscatter gauges, smoke detectors, fill height detectors and in measuring ash content of coal.
Caesium-137:
Used for radiotracer technique for identification of sources of soil erosion and deposition, in density and fill height level switches.
Chromium 57:
Used to label sand to study coastal erosion.

Cobalt-60, Lanthanum-140, Scandium-46, Silver-110m, Gold-198:
Used together in blast furnaces to determine resident times and to quantify yields to measure the furnace performance.

Cobalt-60:
Used for gamma sterilisation, industrial radiography, density and fill height switches.

Gold-198 & Technetium-99m:
Used to study sewage and liquid waste movements, as well as tracing factory waste causing ocean pollution, and to trace sand movement in river beds and ocean floors.

Gold-198:
Used to label sand to study coastal erosion.

Hydrogen-3 (Tritiated Water): Used as a tracer to study sewage and liquid wastes

Iridium-192
Used in gamma radiography to locate flaws in metal components.

Krypton-85:
Used for industrial gauging.

Manganese-54:
Used to predict the behaviour of heavy metal components in effluents from mining waste water.

Nickel-63
Used in light sensors in cameras and plasma display, also electronic discharge prevention and in electron capture detectors for thickness gauges.

Selenium-75:
Used in gamma radiography and non-destructive testing.

Strontium-90:
Used for industrial gauging.

Thallium-204:
Used for industrial gauging.

Ytterbium-169:
Used in gamma radiography and non-destructive testing.

Zinc-65:
Used to predict the behaviour of heavy metal components in effluents from mining waste wate

Q7. Classify vitamins. Write structure , sources and applications of vitamin A and vitamin D.

Each vitamin is typically used in multiple reactions, and, therefore, most have multiple functions.

Classes of vitamins, sources and applications of vitamin A and vitamin D are shown in the table given below:-

Vitamin generic descript or name	Vitamerchemical name(s) (list not complete)	Solubility	Recommended dietary allowances (male, age 19–70)[7]	Deficiency disease	Upper Intake Level (UL/day)[7]	Overdose disease	Food sources
Vitamin K	phylloquinone,menaquinones	Fat	120 µg	Bleeding diathesis	N/D	Increases coagulation in patients taking warfarin.[19]	Leafy green vegetables such as spinach, egg yolks, liver
Vitamin E	Tocopherols,tocotrienols	Fat	**15.0 mg**	Deficiency is very rare; mild hemolytic anemiain newborn infants.[17]	1,000 mg	Increased congestive heart failure seen in one large randomized study.[18]	Many fruits and vegetables, nuts and seeds
Vitamin D	Cholecalciferol,Ergocalciferol	Fat	10 µg[16]	Rickets andOsteomalacia	50 µg	Hypervitaminosis D	Fish, eggs, liver, mushrooms
Vitamin C	Ascorbic acid	Water	**90.0 mg**	Scurvy	2,000 mg	Vitamin C megadosage	Many fruits and vegetables, liver

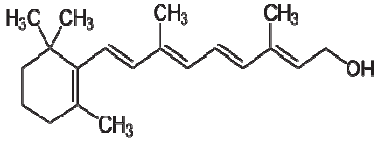
Vitamin generic descript or name	Vitamerchemical name(s) (list not complete)	Solubility	Recommended dietary allowances (male, age 19–70)[7]	Deficiency disease	Upper Intake Level (UL/day)[7]	Overdose disease	Food sources
Vitamin B_9	Folic acid, folinic acid	Water	**400 µg**	Megaloblastic anemiaand Deficiency during pregnancy is associated with birth defects, such as neural tube defects	1,000 µg	May mask symptoms of vitamin B_{12} deficiency; other effects.	Leafy vegetables, pasta, bread, cereal, liver
Vitamin B_7	Biotin	Water	30.0 µg	Dermatitis, enteritis	N/D		Raw egg yolk, liver, peanuts, certain vegetable
Vitamin B_6	Pyridoxine,pyridoxamine,pyridoxal	Water	**1.3–1.7 mg**	Anemia[14] peripheral neuropathy.	100 mg	Impairment ofproprioception, nerve damage (doses > 100 mg/day)	Meat, vegetables, tree nuts, bananas
Vitamin B_5	Pantothenic acid	Water	5.0 mg[12]	Paresthesia	N/D	Diarrhea; possibly nausea and heartburn.[13]	Meat, broccoli, avocados
Vitamin B_3	Niacin, niacinamide	Water	**16.0 mg**	Pellagra	35.0 mg	Liver damage (doses > 2g/day)[11] and other problems	Meat, fish, eggs, many vegetables, mushrooms, tree nuts
Vitamin B_2	Riboflavin	Water	**1.3 mg**	Ariboflavinosis	N/D		Dairy products, bananas, popcorn, green beans, asparagus

Vitamin generic descript or name	Vitamerchemical name(s) (list not complete)	Solubility	Recommended dietary allowances (male, age 19–70)[7]	Deficiency disease	Upper Intake Level (UL/day)[7]	Overdose disease	Food sources
Vitamin B_{12}	Cyanocobalamin,hydroxycobalamin,methylcobalamin	Water	**2.4 µg**	Megaloblastic anemia[15]	N/D	Acne-like rash [causality is not conclusively established].	Meat and other animal products
Vitamin B_1	Thiamine	Water	**1.2 mg**	Beriberi, Wernicke-Korsakoff syndrome	N/D[9]	Drowsiness or muscle relaxation with large doses.[10]	Pork, oatmeal, brown rice, vegetables, potatoes, liver, eggs
Vitamin A	Retinol, retinal, and four carotenoids including beta carotene	Fat	**900 µg**	Night-blindness,Hyperkeratosis, andKeratomalacia[8]	3,000 µg	Hypervitaminosis A	Orange, ripe yellow fruits, leafy vegetables, carrots, pumpkin, squash, spinach, liver, soy milk, milk

Vitamin	Food source
Vitamin B_1 (Thiamine)	Rice bran
Vitamin A (Retinol)	Cod liver oil
Vitamin C (Ascorbic acid)	Citrus, most fresh foods
Vitamin D (Calciferol)	Cod liver oil

Vitamin	Food source
Vitamin B_2 (Riboflavin)	Meat, eggs
(Vitamin E) (Tocopherol)	Wheat germ oil, unrefined vegetable oils
Vitamin B_{12} (Cobalamins)	liver,eggs, animal products
Vitamin K_1 (Phylloquinone)	Leafy green vegetables
Vitamin B_5 (Pantothenic acid)	Meat, whole grains, in many foods
Vitamin B_7 (Biotin)	Meat, dairy products, eggs
Vitamin B_6 (Pyridoxine)	Meat, dairy products
Vitamin B_3 (Niacin)	Meat, eggs, grains
Vitamin B_9 (Folic acid)	Leafy green vegetables

Structure of Vitamin –A is



Structure of vitamin D is