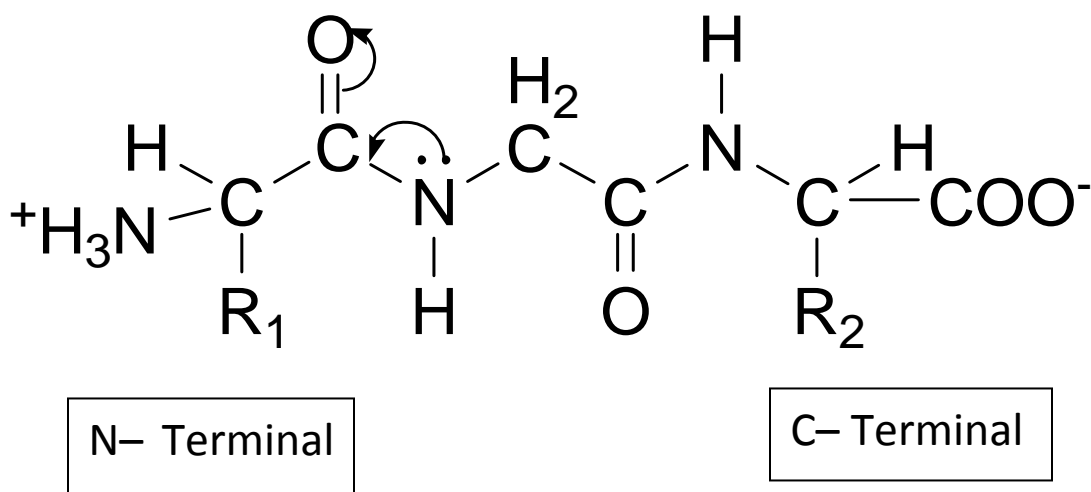


# Biochemistry

## Amino acids

### Peptides and peptide bond: -

The L –  $\alpha$  – amino acids can be polymerized by peptide bond to form peptide or protein. The reaction between  $\alpha$  – amino group and  $\alpha$  – carboxyl group is a simple elimination of  $H_2O$  molecules, when peptides are drawn; their amino terminal written on **left** and carboxyl group to **right**.



The peptide usually written in a *Zigzag* form with repeating sequence of backbone atoms: -

$\alpha$  – nitrogen,  $\alpha$  – carbon, carbonyl carbon.

Amino acid unit in a peptide is called a **residue** (the part after losing a hydrogen atom from its amino group and a hydroxyl moiety from its carboxyl group).

Peptides are named as derivatives of the carboxyl terminal aminoacyl residue. For example: -

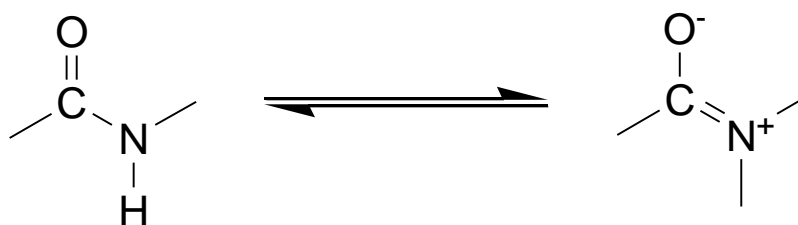
Lys – Leu – Tyr – Glu

Lysyl – leucyl – tyrosyl – glutamine

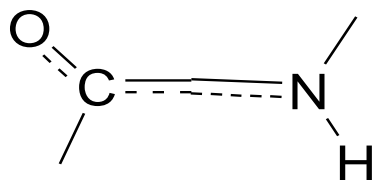
The sequence of amino acids in peptides or protein determined the primary structure, the mutation of DNA which coded amino acid may result in insertion or elimination of residues in peptides or protein and this often effect the biologic activity (like alcohol intolerance or sickle cell disease). Many inherited metabolic errors involve a single change of amino acid sequence.

### Peptide bonds: -

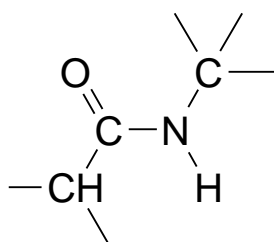
The peptide bond has partial double bond character from  $\alpha$  – carbonyl and  $\alpha$  – nitrogen.



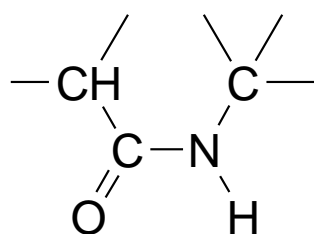
Because of resonance stabilization and hence rigidity on the C – N bond



- Carbonyl group and amine group are parallel.
- There is very little twisting about C – N bond.
- The groups of atoms of peptide bond could be existing in two possible conformations.



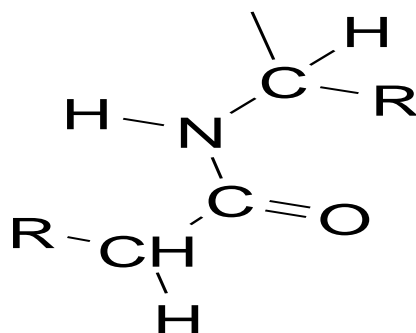
trans



cis

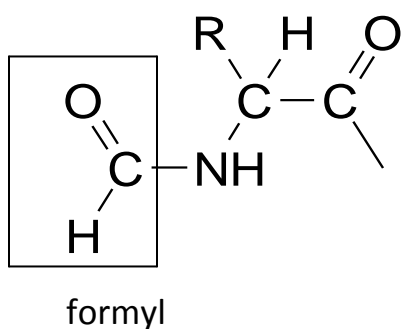
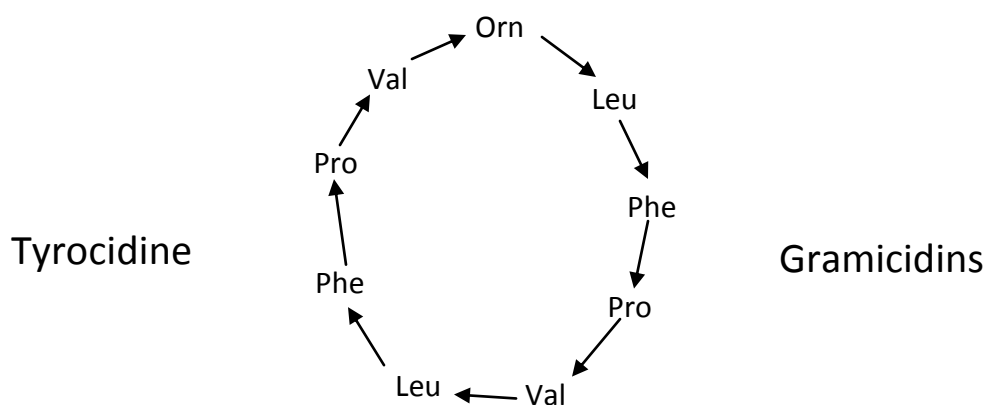
In fact, the **trans** form is usually favored because in cis conformation the R bulky group on adjacent  $\alpha$  – carbon usually interfere “steric effect” the exception is the Pro.

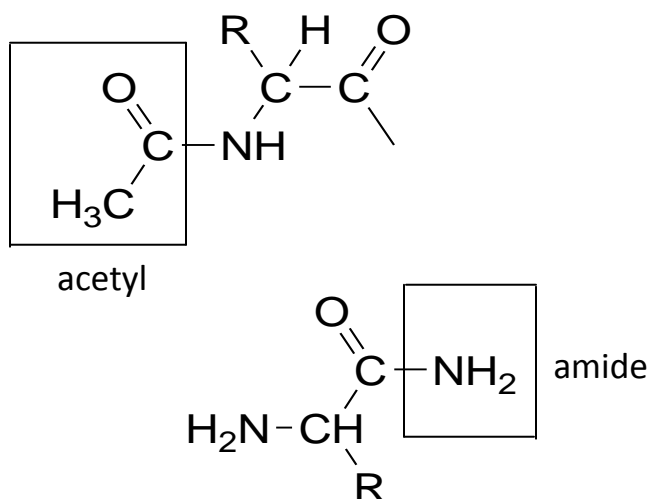
- Peptide bond fixed in a plane, the plane can rotate about  $\alpha$  – carbon



Peptides can be simple *dipeptide* and amino acid residues fewer than 10 these called *oligopeptides* and long peptides more than 10 amino acids called *polypeptides*, and longer than 100 amino acids called *protein*.

There is some cyclic oligopeptides in which N & C terminal have been linked like “antibiotic polypeptide from *Bacillus*” this peptide form complexes with metal ions and disruption transport across the cell membrane and killing certain bacteria; N terminal always free but sometime blocked by formyl or acetyl group.

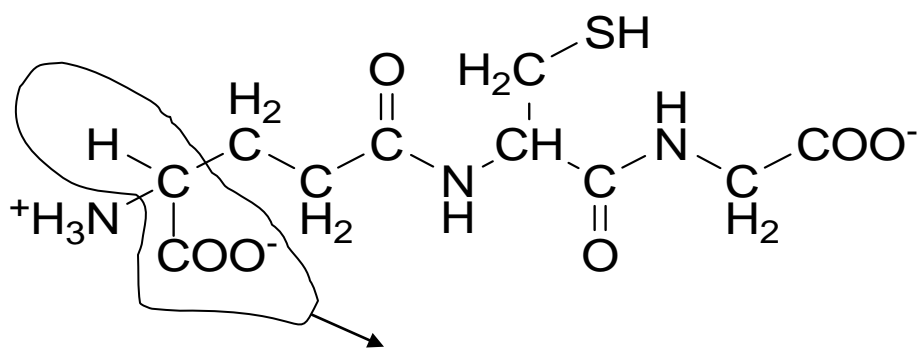




## Biologically important peptides: -

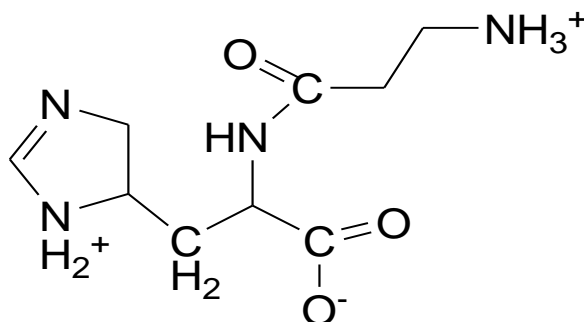
These peptides formed either from hydrolysis of large proteins or synthesized in the body: -

1. **Glutathione (GSH):** this is active tripeptide consisting of  $\gamma$  – glutamic acid – cysteinyl – glycine



- This peptide requires Non  $\alpha$  – peptide bond
- Participate in formation of the correct disulfide bonds for peptides and proteins function in oxidation – reduction system.
- Participate in metabolism of xenobiotics (foreign compound to body) like drugs, carcinogens and chemical.

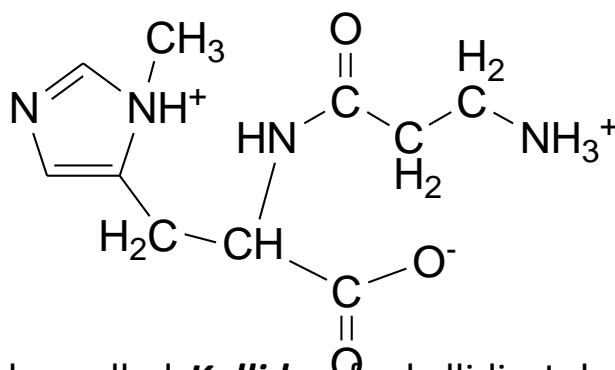
**2. Carnosine:** which is water soluble, dipeptide of  $\beta$  – Alanine and Histidine



This dipeptide occur in human skeletal muscle

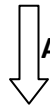
**Anserine:** is water soluble dipeptide N – methyl carnosine which derived from diet and occur in skeletal muscle for the contract activity.

Both carnosine and anserine chalet copper and enhance copper uptake, also buffers the pH of anaerobically contracting skeletal muscle and activate **myosin ATPase** activity.



**3. Kinins:** also called **Kalliden** {a. kallidin I, b. kallidin II}. They are two related peptides found in body, one is called **bradykinin** with 9 amino acids and the other one is **lysylbradykinin**.

Kallidin II: Lys – Arg – Pro – Pro – Gly – Phe – Ser – Pro – Phe – Arg



Amino peptidase

Kallidin I: Arg – Pro – Pro – Gly – Phe – Ser – Pro – Phe – Arg

9 amino acids

The action of kinins resemble those of **histamine** as vasodilator, kinins relax vascular smooth muscle and lowering blood pressure and increase capillary permeability, they also mediate the production of **prostaglandin E<sub>2</sub>** from arterial wall.

**4. Oxytocin and vasopressin:** these two cyclic peptide hormones which secreted from pituitary gland.

**Oxytocin:** is a peptide with 9 amino acids secreted by posterior pituitary and act on uterine muscles during labor.

**Vasopressin:** this hormone called also (ADH) anti diuretic hormone, which effect the reabsorption of H<sub>2</sub>O from the distal and collection tubule of kidneys.

**5. Angiotensins:** there are two kinds of angiotensins {angiotensin I & angiotensin II}

**Angiotensin I:** is a peptide with 10 amino acids which result from the action of the renin (the proteolytic enzyme which release from kidneys) on the angiotensinogen to produce angiotensin I.

Angiotensin I converted to angiotensin II (8 amino acids) by the angiotensin – converting enzyme (ACE) which found mainly in lungs and remove two amino acids from angiotensin I.

Angiotensin II has a greater effect on blood pressure by causing the vasoconstriction of the arterioles and also stimulates the secretion of **aldosterone** which promotes sodium retention.

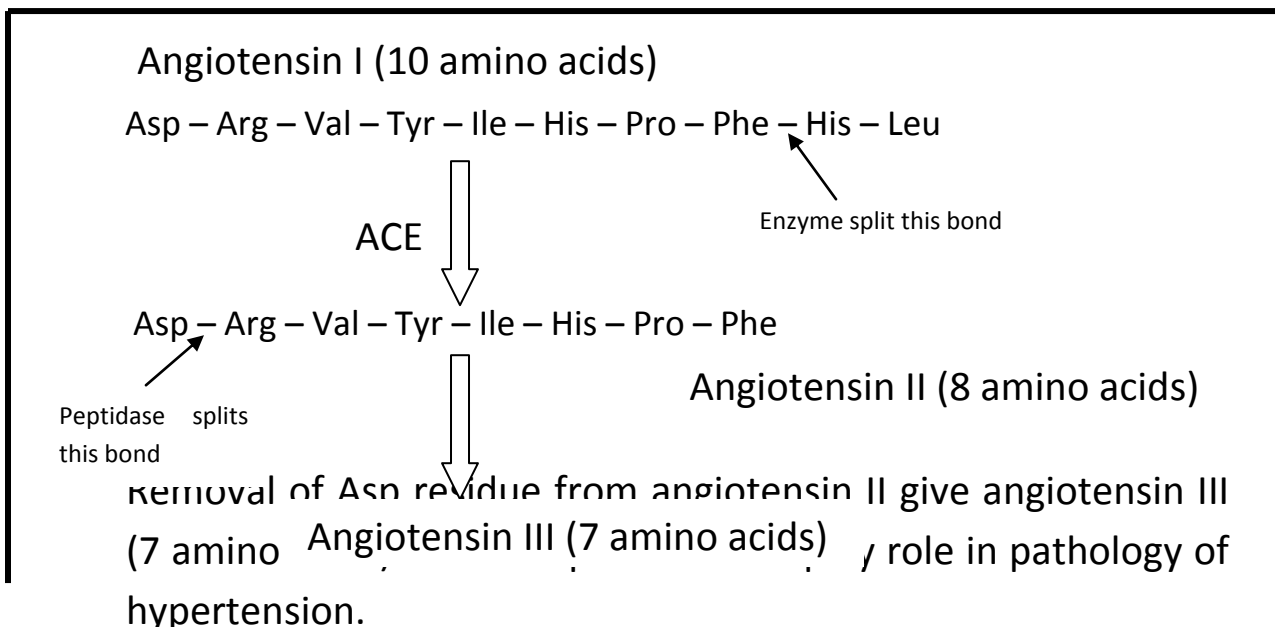
Angiotensin II stimulates thirst, dilator of blood vessels of voluntary muscles and brain.

Renin – angiotensin system is the major controlling mechanism of aldosterone secretion which increases sodium reabsorption in the distal tubule of the kidneys.

**Renin:** this enzyme stimulated by **hypotension** and **sodium depletion**.

Angiotensin I has a slight effect on blood pressure.

**Angiotensinogen:** is globulin fraction of plasma which produced from liver.



In human the plasma level of angiotensin II is four times greater than of angiotensin III.



**6. Gastrin, secretin and pancreozymin:** these three gastrointestinal peptides act as hormones that stimulate secretion of bile and other enzymes of digestive juices.

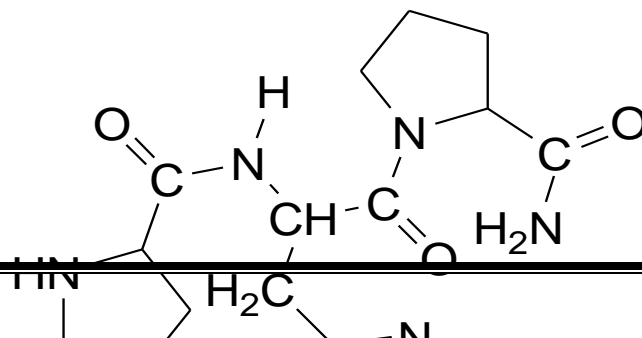
**7. Corticotropin or ACTH:** this peptide is a hormone secreted from pituitary gland which contains 39 amino acids stimulates cortisol secretion, ACTH is controlled by corticotropin releasing hormone (CRH) from hypothalamus. ACTH secretion shows diurnal variation; the highest level occurring in the early morning and lowest levels in late evening.

Some polypeptides are a precursor for small polypeptide like:

- $\beta$  – lipotropin is precursor for MSH (melanocyte – stimulating – hormone) and endorphins.
- $\beta$  – MSH hormone made up of the 17 amino acids also secreted from pituitary gland [this is not normally released in the blood].
- Lipotropin stimulates the release of fatty acids from adipose tissue.

### Hypothalamic – releasing factors: -

They are low molecular weight polypeptides and they regulation of pituitary secretion, like: TRH



8. **Opiate peptides:** the enkephalins and endorphins (endogenous morphine) are peptide with opiate effects, because they bind to opioid receptors even though their structure is unrelated to that of morphine. Opiate peptide occurs widely throughout the central nervous system and appears to be neurotransmitters and play a role in memory and in the response to stress and pain.
9. **Antibiotics:** like penicillin, gramicidin, polymyxin, bacitracin, actinomycins, and chloramphenicol all are antibiotics with peptides structure.