

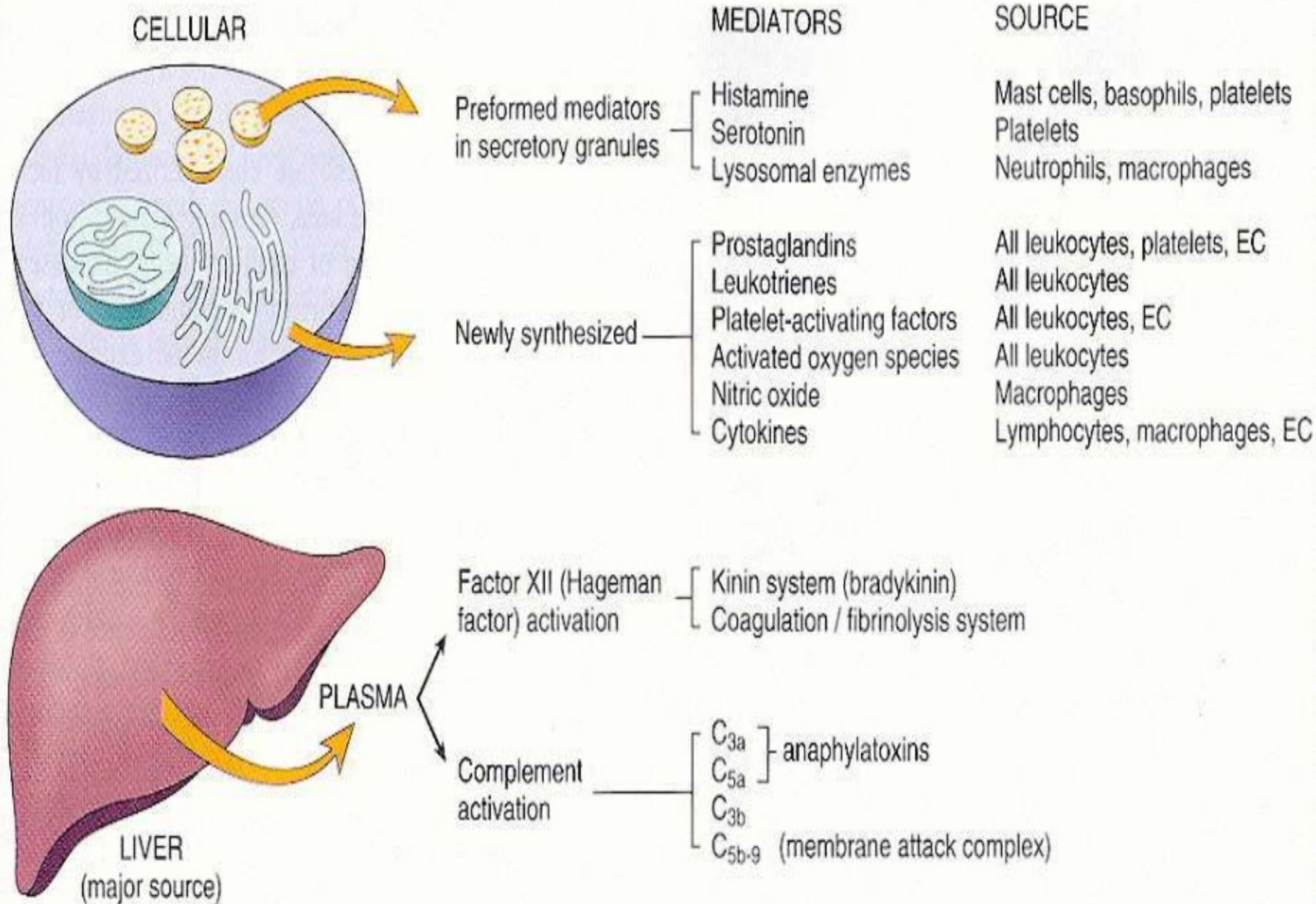
# ***Mediators of inflammation***

- Definition: Any messenger that acts on blood vessels, inflammatory cells, or other cells to contribute to an inflammatory response.

# ***Classification***

- Cell derived mediators
- Plasma derived mediators





# 1. Cell derived mediators

a) vasoactive amines (serotonin, histamine)

b) arachidonic acid metabolites

- cyclooxygenase pathway
- lipoxygenase pathway

c) Lysosomal components

d) Platelet activating factor

e) Cytokines (IL-1, TNF- $\alpha$ , TNF- $\beta$ , IF- $\gamma$ , Chemokines)

f) Nitric oxide and oxygen metabolites



# a) Vasoactive amines

## Histamine :-

- Stored in granules of mast cells, basophiles and platelets.
- Released by the stimuli of various agents like Heat, Cold, Irradiation, Irritant chemicals, Anaphilatoxins, Interleukins,.. etc.
- Actions ; Vasodilation
  - ↑ Vascular permeability
  - Itching and pain

## Serotonin/5-hydroxy tryptamine :-

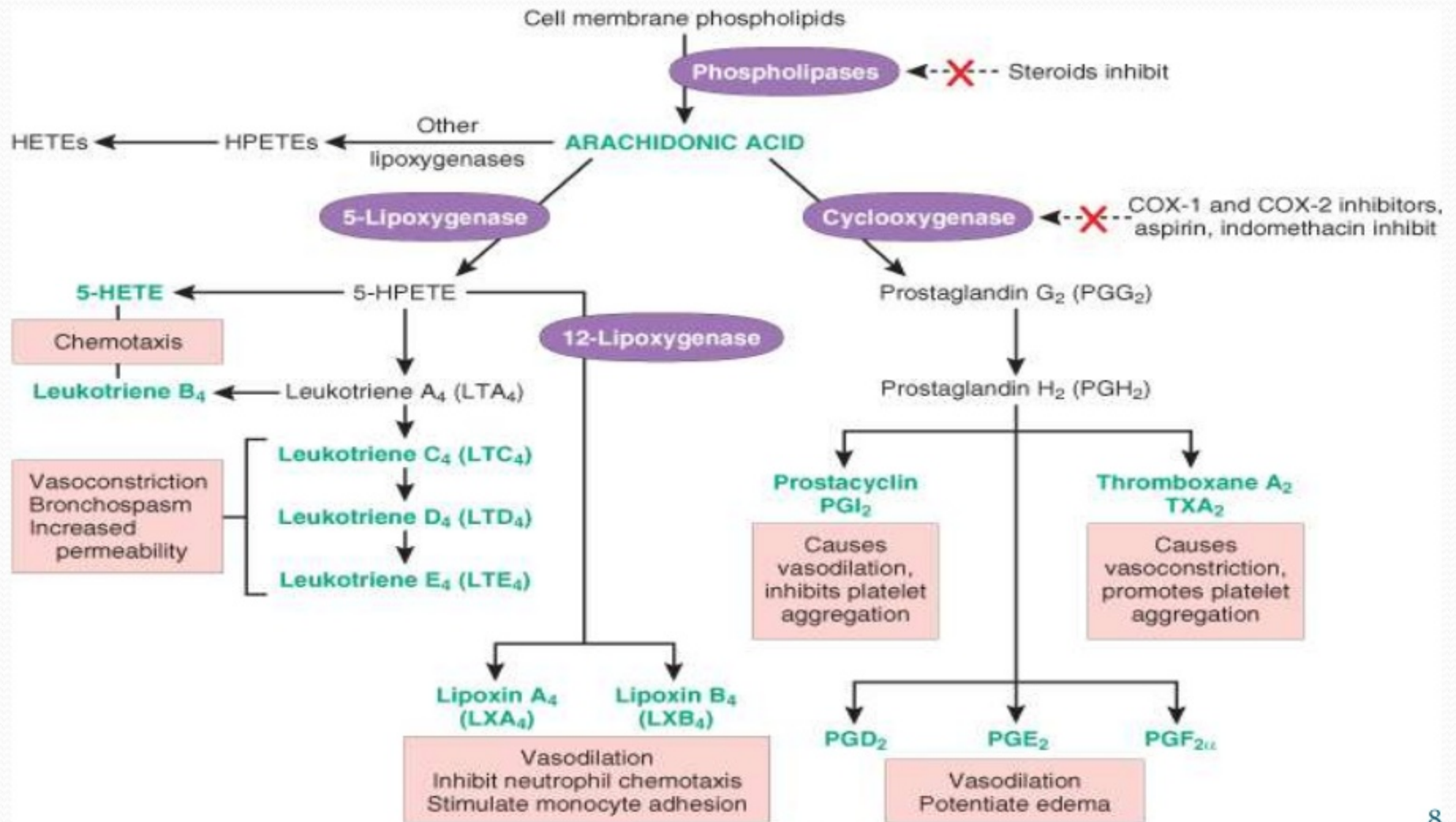
- Present in chromafin cells of GIT, Spleen, Nervous tissue, Mast cells, Platelets.
- Actions ; Similar to Histamine, but less potent
  - Vasodilation
  - ↑ Vascular permeability



# b) Arachidonic acid Metabolites

Lipoxygenase pathway

Cyclo-oxygenase pathway



## c) Lysosomal components

- Source :- Neutrophils and monocytes
- Potent mediators
- Degradation of bacterial and extracellular components
- Chemotaxis
- Release of acid proteases, collagenase, elastase, plasminogen activator



## d) Platelet activating factor

- Phospholipid derived mediator
- Released from :- Platelets, basophil, mast cells, neutrophils macrophages, endothelial cells
- Actions :-
  - ↑ Vascular permeability
  - Vasoconstriction
  - Vasodilatation
  - Bronchoconstriction
  - Adhesion of leukocytes to endothelium
  - Chemotaxis, degranulation

## e) Cytokines

“Cytokines are a diverse group of small protein molecules with potent biological activity whose main function is in the regulation of immune responses.”

Main Cytokines are :-

- Interleukins
- Interferons
- Tumor necrosis factor
- Chemokines
- Transforming growth factor-beta
- Adipokines- leptin & adiponectin



## Actions :-

- ↑ Adhesion of leucocytes to endothelium
- ↑ Synthesis of Prostacyclin, which is a vasodilator and anti aggregator of platelets
- ↑ Synthesis of PAF and thrombogenic effect on endothelial surface

## f) Nitric oxide and oxygen metabolites

- Endothelium derived relaxing factor
- Macrophages, endothelial cells, neurons

Actions :-

Vasodilation

Anti-platelet activating agent

Microbicidal action

- $H_2O_2$  , Superoxide, Toxic NO products produced by activated neutrophils and macrophages

Actions :-

Endothelial cell damage, tissue damage and  $\uparrow$ vascular permeability



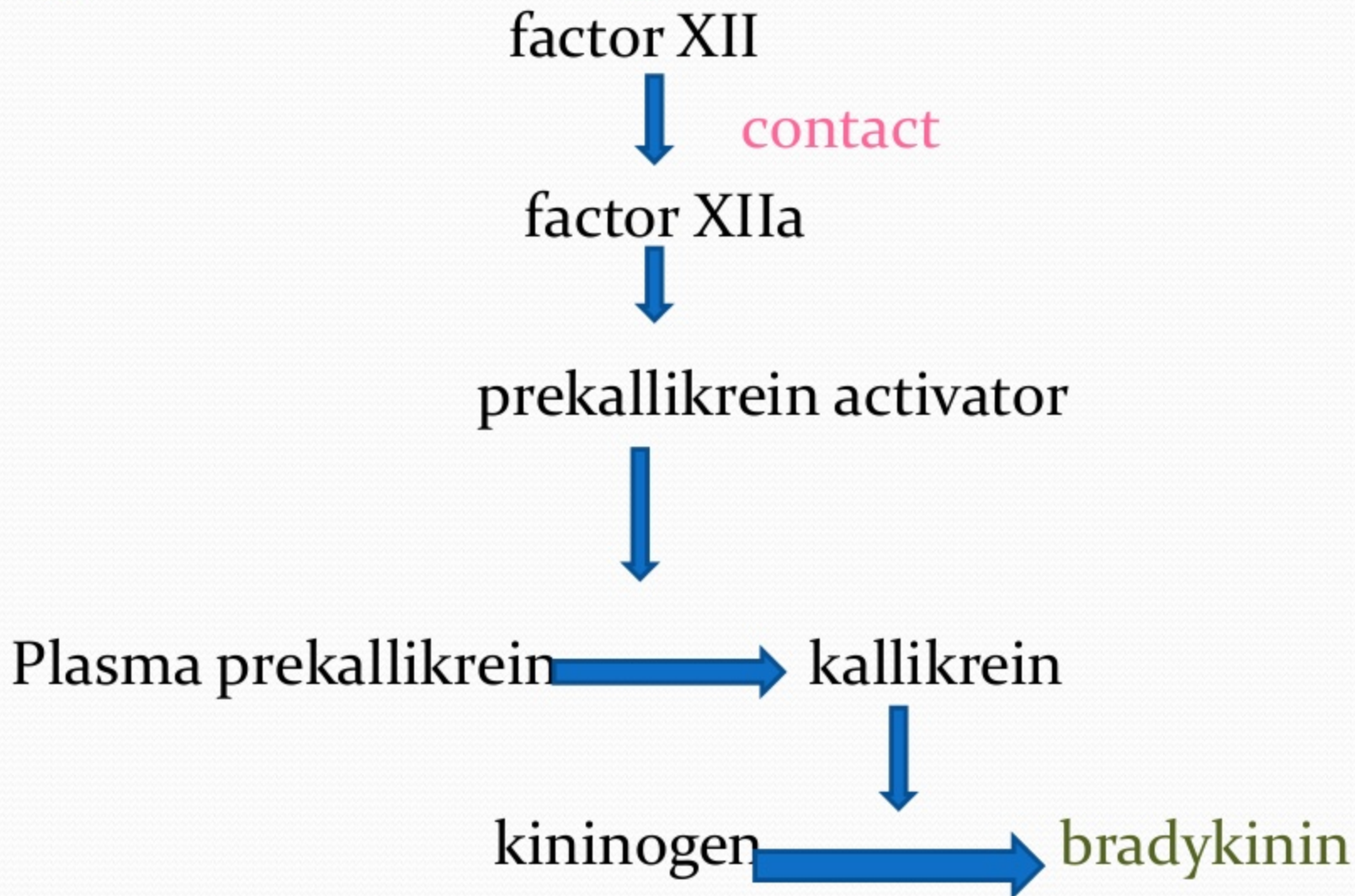
## 2. Plasma derived mediators

- a) The kinin system
- b) The clotting system
- c) The fibrinolytic system
- d) The complement system

- 4 interlinked systems
- Hageman factor(factor XII)
- End product of clotting ,fibrinolytic ,kinin system will activate complement system.



# a) The kinin system

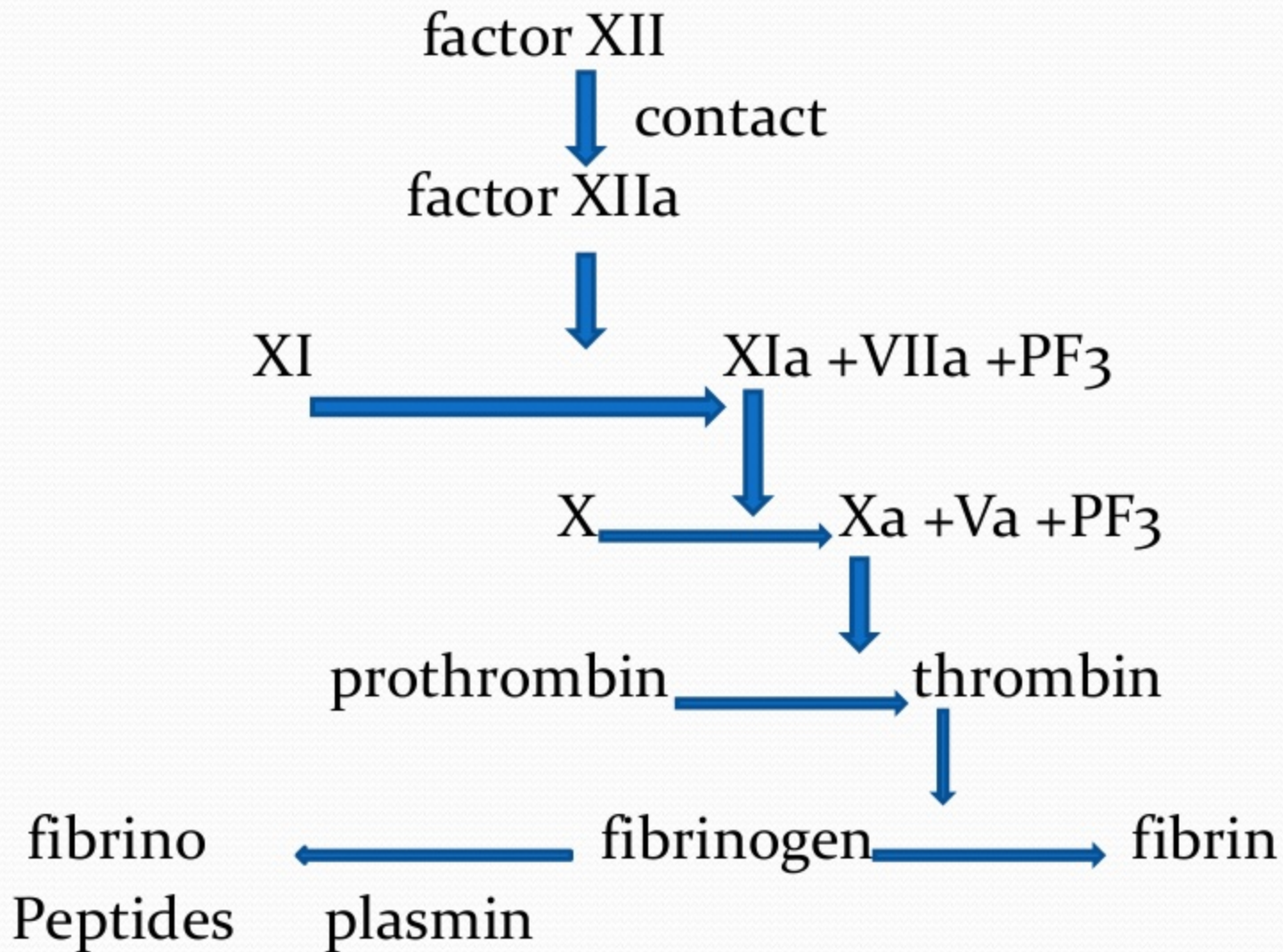


## Actions :-

- ❖ Smooth muscle contraction
- ❖ Vasodilation
- ❖ ↑vascular permeability
- ❖ pain



## b) Clotting system



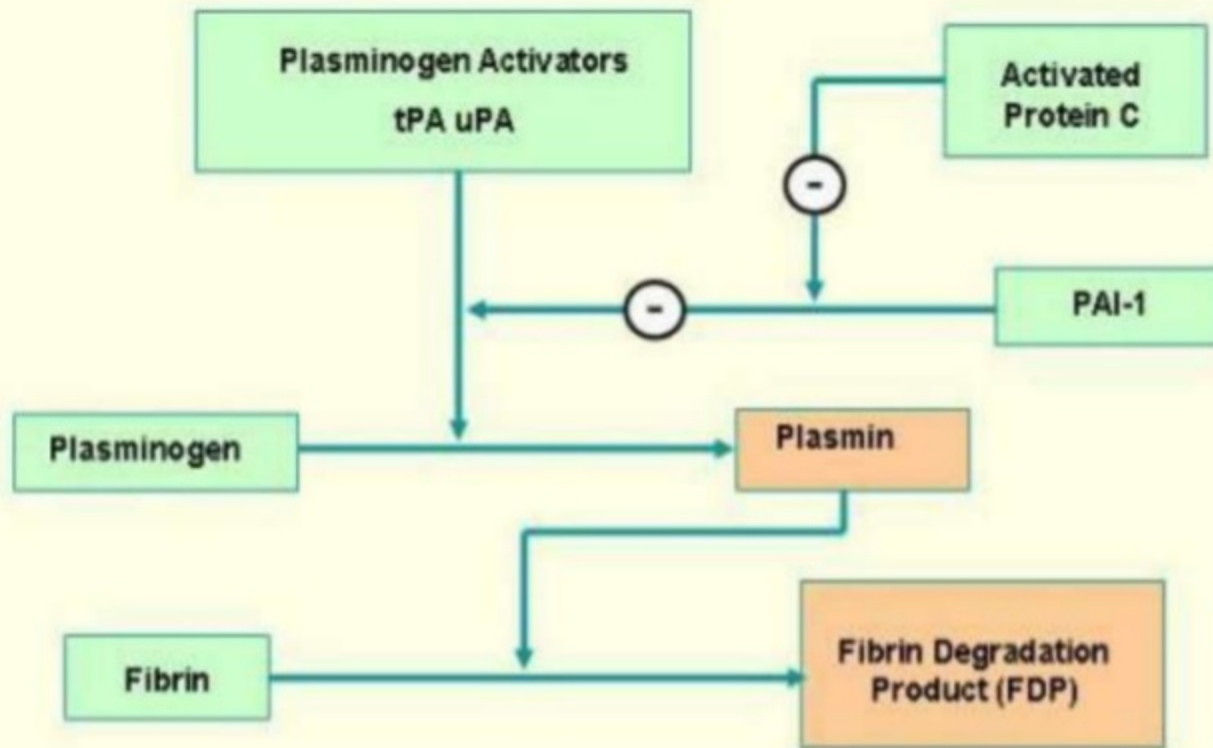
## Actions :-

- Increase vascular permeability
- Chemotaxis for leucocytes
- Anticoagulant activity



# C) Fibrinolytic system

## Fibrinolytic System



## Actions :-

- Activation of factor XII to form prekallikrein activator that stimulates kinin system to generate bradykinin
- Splits off complement c3 to form c3a, which is permeability factor
- Degrades fibrin to split products, they increase vascular permeability



## D) Complement system

- Product of complement system is anaphylatoxins c3a and c5a.
- Potency is  $c3a > c5a > c4a$
- Actions:- release histamine from mast cells and basophils
- C5a is chemotactic for leucocytes.
- Membrane attack complex cause pores in cell of invading microbes.