

**Eicosanoids** are less common lipids and are derivatives of arachidonic acid. They are **cellular signaling agents**. They include:

- Prostaglandins – involved in an inflammatory response
- Leukotrienes – responsible for allergic responses and asthma.
- Thromboxanes – involved in blood clotting

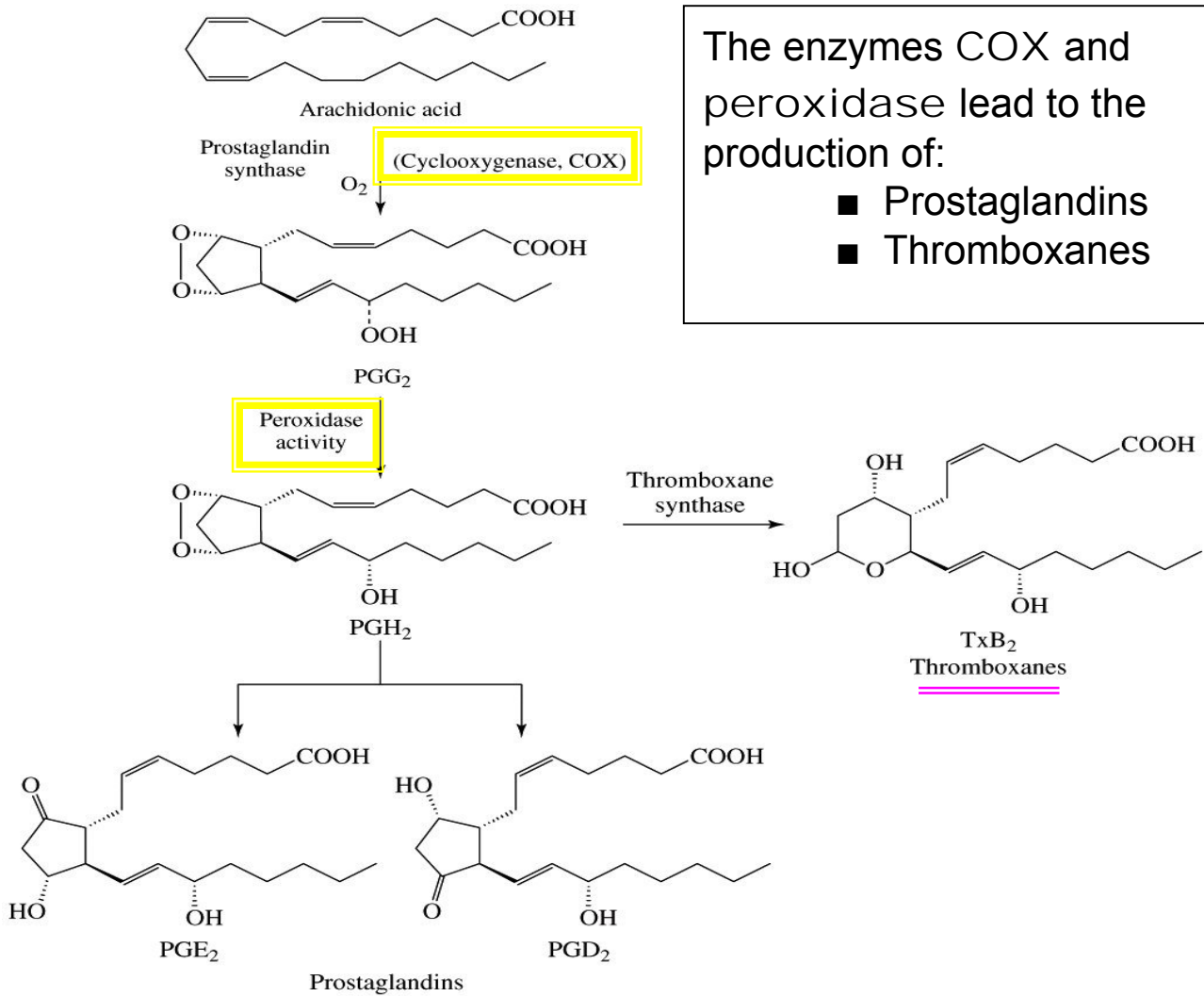
### Table 8.4

#### Biological Activities of the Eicosanoids

1. Initiate the inflammatory response, pain, and fever associated with injury (cuts, scrapes, blisters, etc.) and diseases (osteoarthritis and rheumatoid arthritis).
2. Promote the blood clotting process (platelet aggregation) and regulate blood pressure (some prostaglandins are vasodilators).
3. Control of some reproductive functions, for example, inducing labor, and a possible role in male infertility.
4. Regulate temperature and the sleep/wake cycle in animals.
5. Promote smooth muscle contraction.

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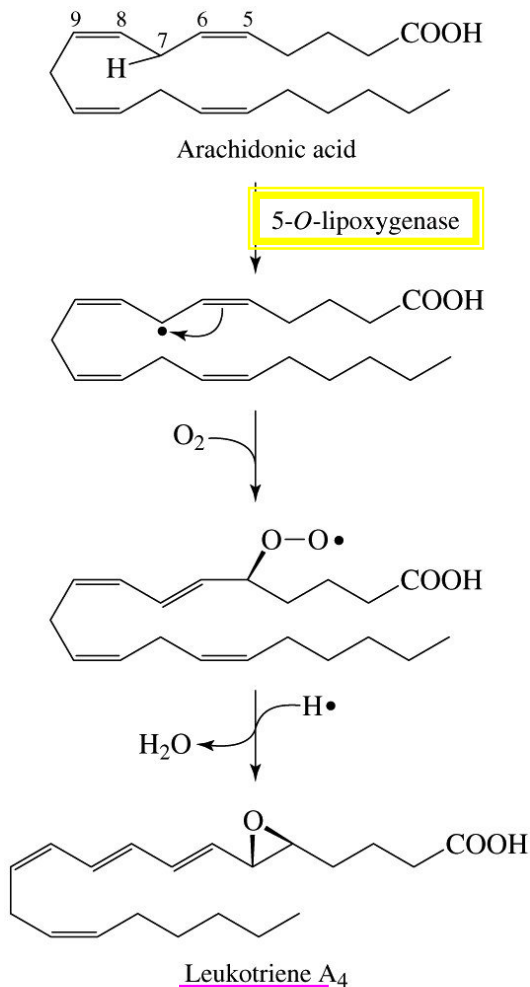
As stated above, eicosanoids are derivatives of arachidonic acid. Its precursor, linoleic acid (the essential  $\omega$ -6 fatty acid) is stored as a fatty acid in cell membranes and released by the action of a **phospholipase** enzyme.



The enzymes COX and peroxidase lead to the production of:

- Prostaglandins
- Thromboxanes

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The enzymes lipoxygenase leads to the production of:

- Leukotrienes

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So to treat inflammation (caused by prostaglandins), COX inhibitors are used because by blocking COX, we stop PG synthesis at its first step, which lowers the level of PGs and so lessens the inflammatory response.

Classical NSAIDs (naproxen, ASA, ibuprofen, etc) act as nonspecific COX inhibitors, blocking the production of PGs.

It is thought that PGs play a protective role in the stomach by synthesizing mucopolysaccharides. These glycosides protect the stomach lining from HCl. When patients are on COX inhibitors for extended periods, stomach ulcers may develop.

\*Note the structure of NSAIDs. All have a carboxyl group (COOH) except for Acetaminophen which acts poorly on inflammation.

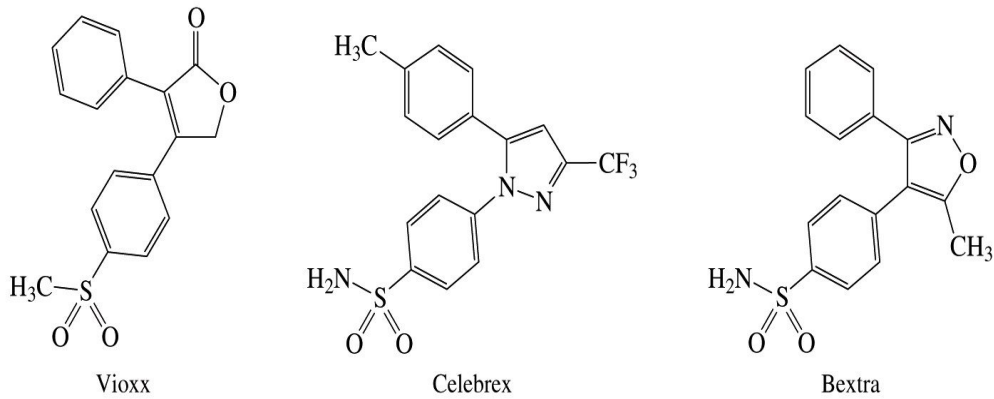


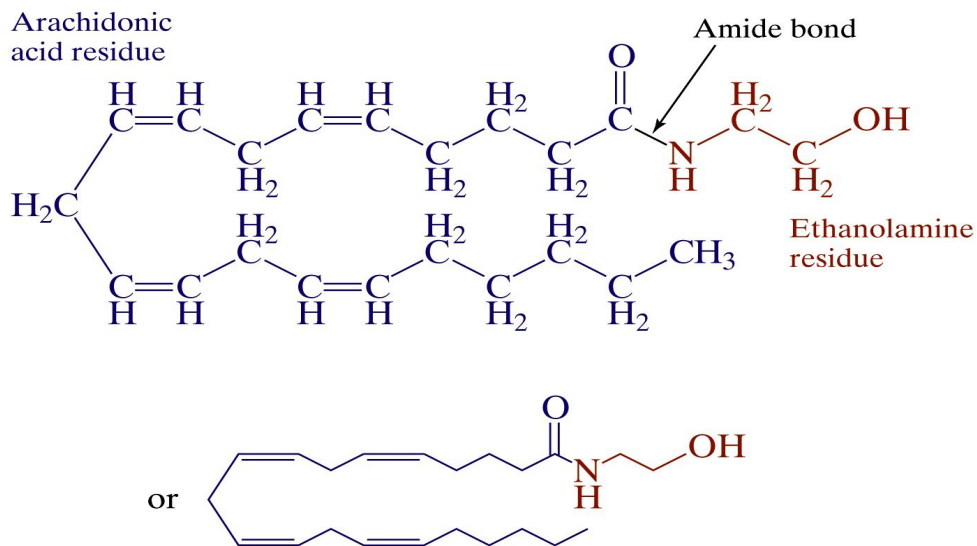
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Newer drugs, such as Celebrex and Vioxx act specifically on COX-2 in an attempt to avoid the stomach ulcer side-effect thought to be caused specifically by inhibiting COX-1. COX-2 inhibitors have been linked to heart attack and death in patients and Vioxx was recently taken off the market.

Celebrex has been thought to inhibit cancer growth.

Arachidonic acid is also involved in the biosynthesis of anandamide, a cannabinoid neurotransmitter found naturally in the brain. Anandamide binds to cannabinoid receptors in the brain, lessening pain and producing feelings of euphoria.

Anandamide is found naturally in marijuana and chocolate.



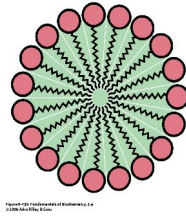
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# LIPID MEMBRANES

The type of lipids (saturated or unsaturated, fatty acid or phospholipid) determines the whether the lipids will form:

- Micelles or
- Lipid bilayers

**Fatty acids form micelles** because they're smaller (one nonpolar tail) and there is less steric hindrance.



The critical micelle concentration is the concentration of fatty acids required to form micelles.

- This concept is applied in laundry detergent.
  - Micelles are formed and then broken apart by the washing machine's agitation which disrupts the micelle's interior London forces. The micelles then reform with dirt inside.
  - If you're cheap and don't use enough detergent (<critical micelle concentration) your clothes will not get clean.

**Phospholipids** cannot easily form micelles due to the presence of two nonpolar tails and so **form lipid bilayers**.

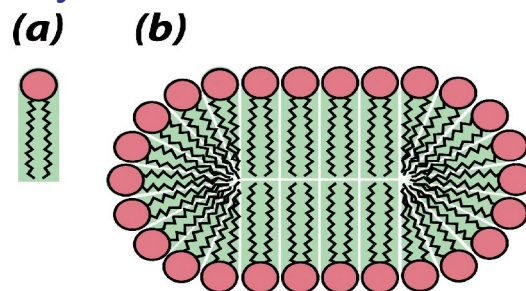
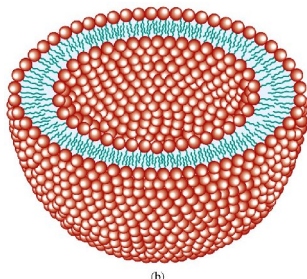
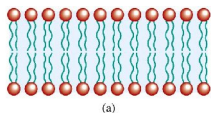


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The phosphate head is hydrophilic and faces the solution while the nonpolar tail is pushed to the hydrophobic center.



Other structures may also form, such as a liposome, which is a hollow sphere like structure which an aqueous center. **Vesicles** are thought to exist as this structure.



The phospholipids bilayer is semipermeable (some molecules may pass, others may not).

- Water and other small polar molecules can pass through
- Small nonpolar molecules may pass through
- Cations may NOT pass
- Anions might pass (some do, some don't)

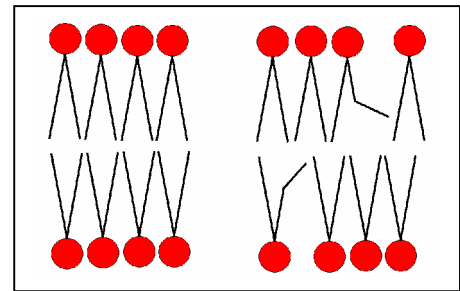
The structure of the phospholipids bilayer is said to be fluid or chaotic. The more disordered the membrane, the higher the fluidity.

- Protein function depends on membrane fluidity.
- Organisms maintain optimal membrane fluidity

### Fluidity can be regulated by:

#### ■ Type of fatty acid

- More unsaturated fatty acids
  - Very fluid → high permeability
- More saturated fatty acids
  - Low fluidity → low permeability



#### ■ London forces

- Weak London forces,
  - very fluid → high permeability
- Strong London forces,
  - low fluidity → low permeability

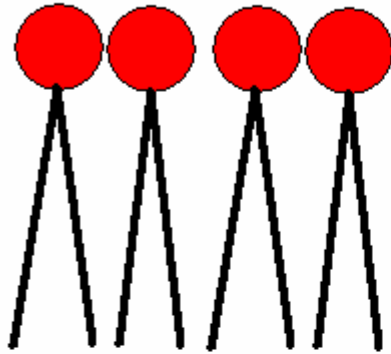
#### ■ Temperature

- Depends on transition temperature (temp of phase change)
  - Below transition temp,
    - becomes a gel-like solid, low fluidity → low permeability
  - Above transition temp,
    - liquid crystal, very fluid → high permeability
- Transition temp increases with chain length and saturation

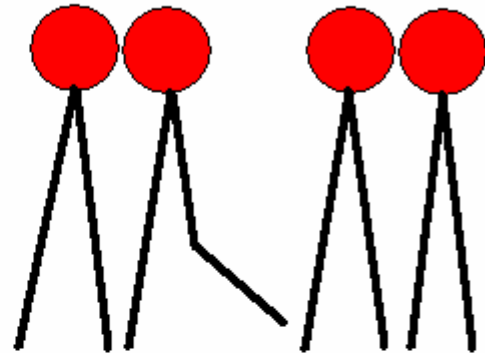
#### ■ Cholesterol insertion (see pic below)

- Can also serve to broaden the temp change of the phase transition

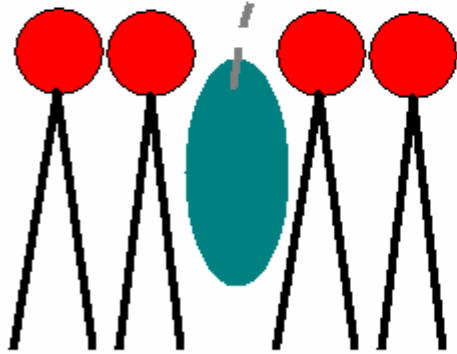
lipid bilayer consisting of saturated fats



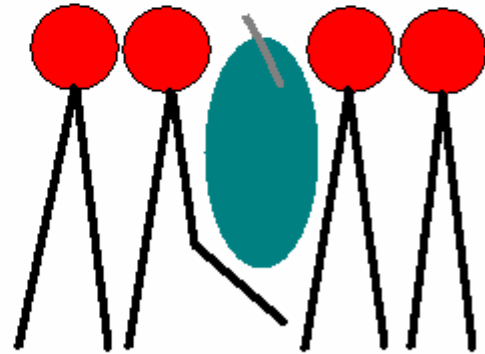
lipid bilayer consisting of UNsaturated fats



steroid



upon cholesterol insertion:  
\* fluidity increases  
\* permeability increases



upon cholesterol insertion:  
\* fluidity decreases  
\* permeability decreases