

fluid for aspirin.

6.2.4.2. Oxidation

Oxidation is the removal of electron(s) from a molecule. **Auto-oxidation** is the reaction of compounds and molecular oxygen. Unsaturated fatty acids present in oils and fats are auto-oxidised in the presence of light, atmospheric oxygen, organic peroxides, or traces of heavy metals. **For example**, in the presence of copper ions in 0.002M concentration, the oxidation rate of ascorbic acid increases by the factor of 10^5 .

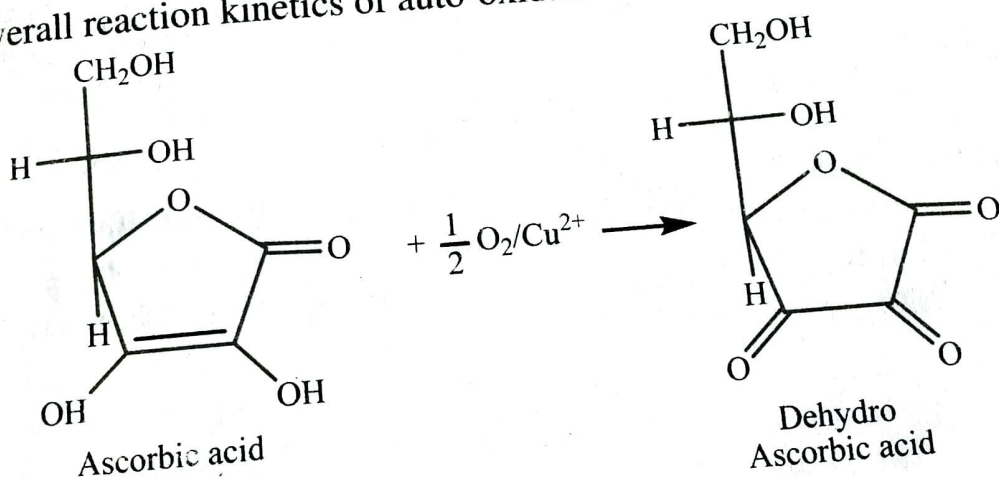
Oxidation reactions are governed by the following principles:

- 1) The oxidation rate increases in the presence of atmospheric oxygen or air.
- 2) The free radicals involved in oxidation results in chain reactions. The energy required for initiating chain reaction is obtained from light.
- 3) Rate of oxidation also increases in the presence of trace metals.
- 4) Oxidation reaction is promoted by chain initiation induced by organic peroxides.
- 5) Drug molecules are available in ionic form or as neutral molecules because they are either weak bases or acids. Oxidation reactions involving neutral molecules are slower than those involving ionic species because oxidation is a solubility related phenomenon.
- 6) Reactions of oxidation are catalysed by H^+ and OH^- ions; However, hydroxyl ions (OH^-) catalyse oxidation reaction faster than the hydrogen ions (H^+). Alkaline solutions react with atmospheric oxygen to form oxides.

Examples of API decomposed by oxidation pathways are:

Arachis oil	Vitamin A
Ethyl oleate	Riboflavin
Clove oil	Vitamin B ₁₂
Cinnamon oil	Ascorbic acid
Promethazine	Morphine
Epinephrine	Prednisolone

The overall reaction kinetics of auto-oxidation of ascorbic acid is shown below:



Preventive Measures

Oxidation reactions take place in the presence of oxygen, trace metals, and H^+ and OH^- ions, therefore, many protective steps has to be taken to terminate the factors promoting oxidation:

- 1) **Anti-Oxidants:** Many natural (e.g., tocopherols, ascorbic acid, etc.) and synthetic anti-oxidants (e.g., butylated hydroxyl anisole, butylated hydroxy toluene, propyl gallate, etc.) are widely used in foods, cosmetics, and drugs to inhibit oxidation reactions. Mechanism of these agents is to break the free radical chain reactions at the chain propagation step.
- 2) **Chelating Agents:** These agents are used in heavy metal-catalysed oxidation reactions. Chelating agents (EDTA, citric acid, and tartaric acid) form complexes with heavy metal ions, thus, free metal ions become unavailable to catalyse the oxidation reaction.

- 3) **Vehicles:** For most of the pharmaceutical preparations, water is used as a solvent or vehicle to dispense the drug. Sometimes water is replaced by other solvents to stabilise the drugs; while water used along with other solvents catalyses the oxidation reactions.
- 4) **Surfactants:** These agents (e.g., polysorbate 80) enhance the oxidation rate of ascorbic acid at low concentration, but protect above its **Critical Micelle Concentration (CMC)**, by entrapping the drugs in spherical micelles. Sometimes, spherical micelles offer a site for surface adsorption of catalytic ions and enhance the rate of reaction.
- 5) **Buffers:** The oxidation reactions catalysed by H^+ or OH^- ions can be controlled by using a buffer solution of appropriate pH. Thus, buffer solutions are helpful in providing maximum stability to the product.
- 6) **Oxygen Free Environment:** Oxidative degradation is catalysed by oxygen, therefore, air is replaced with inert gases (e.g., nitrogen and carbon dioxide) or oxygen free solvents are used for manufacturing drug.
- 7) **Low Temperature Storage:** The pharmaceutical products are stored in a cool place because high temperature enhances the rate of oxidation.

6.2.5. Photolytic Degradation and its Prevention

Photolytic degradation is the degradation of photodegradable molecules caused by the absorption of photons, particularly those wavelengths found in sunlight, such as infrared radiation, visible light, and ultraviolet light. Some molecules get activated by the heat of light which increases the reaction rate.

Drugs which get chemically degraded in the presence of light are **photosensitive or photo-labile drugs**, e.g., riboflavin, tetracycline, and chlorpromazine. Colour fading or colour development are a type of photochemical degradation. Some other **examples** of photochemical reactions are:

- 1) Ergosterol converts into vitamin D when exposed to UV light, and
- 2) Chlorophyll absorbs visible light and undergoes photosynthesis forming carbohydrates and oxygen.

Photodegradation involves combined action of sunlight and air. It involves the process of oxidation (loss of electrons and increase in oxidation state) and hydrolysis (split of chemical bonds by adding water).

Furosemide, acetazolamide, and cyanocobalamin are the **examples** of some phototoxic drugs.

Photolytic degradation can be **prevented** by:

- 1) Packaging of drugs in amber coloured bottles.
- 2) Packaging of drugs in cardboard outers.
- 3) Packaging of drugs with aluminium foil overwraps.

Drugs can be stabilised against photolytic degradation as follows:

- 1) **Temperature:** The drugs should be stored at appropriate temperatures so that thermal acceleration of decomposition is avoided.
- 2) **Light:** Light sensitive drugs should be stored in amber coloured bottles.
- 3) **Humidity:** The drugs should be packed in glass and plastic materials to prevent the exposure of drugs to high humid conditions.
- 4) **Oxygen:** While packing the oxygen-sensitive drugs, the oxygen content of the solution should be kept less and a very little headspace should be left in the bottle above the products.