

# Classification according to maturity biology essay



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## **INTRODUCTION**

The human eye is very nearly spherical, with a diameter of approximately 24 mm (nearly one inch). It consists of three concentric layers, each with its own characteristic appearance, structure and functions. From outermost to innermost, the three layers are the sclera, which protects the eyeball; the choroid, which nourishes the eyeball; and the retina, which detects light and initiates neural messages bound for the brain. The eye is partitioned into two chambers, a small anterior chamber and a larger vitreous chamber. Thus the basic layout consists of three concentric layers, two chambers, iris, pupil and the lens (Ross and Wilson, 2001).

### **Fig. 1 Anatomy of the eye**

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### **The Lens**

One of very important optical element of the eye, the crystalline lens, lies right behind the iris. The lens takes its name from its resemblance to a lentil, or bean. In adults, the lens is shaped about 9 mm in diameter and 4 mm in thickness. The lens consists of three distinct parts: an elastic covering, or capsule; an epithelial layer just inside the capsule; and the lens itself.

The thin, elastic capsule around the lens has two jobs. First, it moderates the flow of aqueous humor into the lens, helping the lens retain its transparency to light. Second, the elastic capsule moulds the shape of the lens varying its flatness and, thereby, the lens optical power. This variant in optical power is called accommodation.

Lens grows throughout the life span; the outer, epithelial layer of lens continues to produce protein fibres that are added to the surface of the lens. Consequently, those protein fibres nearest the centre of the lens are the oldest (some were present at birth), whereas the fibres on the outside are the youngest. Between birth and 90 years of age, the lens quadruples in thickness and attains a weight of 250 mg. In the centre of the lens, the old fibres become more densely packed, producing sclerosis, or hardening, of the lens (Paterson, 1979).

For good vision, the lens must be transparent and light must be able to pass through it easily, without loss or deviation. Like the cornea, this transparency depends on the material out of which the lens is made. Of all the body's parts, the lens has the highest percentage of protein, and its protein fibres are lined up parallel to one another, maximizing the lens transparency to light. Anything that disturbs this alignment such as excess fluid inside the lens reduces its transparency. An opacity (or reduced transparency) of the lens is called a cataract. While some cataracts are minor, barely reducing the transmission of light, others undermine vision to the extent of blindness (Kyselova, 2004).

## **Cataract**

Cataract is the opacification and crystalline formation of eye lens, associated with the breakdown of the eye lens micro-architecture, which interferes with the transmission of light onto the retina. Several biochemical processes for example, calcium deposition, oxidative stress, phase transition, altered epithelial metabolism, crystalline precipitation, calpain-induced proteolysis

and cytoskeletal loss takes place during the development of cataract (Moghaddam, 2005).

## **Fig. 2 Normal, clear lens Fig. 3 Lens clouded by cataract**

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## **Fig. 4 Etiology of cataract (Jacob, 1999)**

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## **TYPES OF CATARACT**

### **A. Acquired cataract**

#### **1. Age related cataract**

##### **a) Morphological classification**

##### **i) Subcapsular cataract**

Anterior subcapsular cataract mainly associated with fibrous metaplasia of the epithelium present below the lens capsule.

Posterior subcapsular cataract lies just in front of the posterior capsule and a clear vacuolated, granular or plaque-like appearance. Near vision is also most often impaired more than distant vision.

ii) Nuclear cataract usually begins as an amplification of the changes most often seen with normal aging lens nucleus. It is often related with increased spherical aberration and also with an increased refractive index leading to myopia. Some elderly patients may consequently be capable to read yet again without spectacles.

iii) Cortical cataract may be associated with the anterior, posterior or equatorial cortex. The opacities begin as clefts and vacuoles between lens fibres because of hydration of the cortex. Both cortical and subcapsular cataracts are white on oblique illumination and show black colouration, silhouetted against the red reflex, on retroillumination.

## **b) Classification according to maturity**

i) An immature cataract means partially opaque lens.

ii) A mature cataract means completely opaque lens.

iii) A hypermature cataract means the leakage of water from the lens it leads to wrinkled and shrunken anterior capsule.

iv) A morgagnian cataract means the total liquefaction of lens cortex like hypermature cataract and it allows the lens nucleus to shrink inferiorly (Hejtmancik, 2004).

## **2. Presenile cataract**

Cataract may develop early in the following conditions,

### **a) Diabetes mellitus**

Typically diabetic cataract is rare. In hyperglycemic conditions, the aqueous humor secretes high level of glucose and this excess of glucose diffuses into the lens. Aldosereductase metabolises glucose to sorbitol, which then accumulates in the lens, resulting in secondary osmotic over hydration of the lens substance. Nuclear opacities are common and tend to grow rapidly. Premature dystrophy may be seen due to decreased pliability of the lens.

## **b) Myotonic dystrophy**

About 90% of patients, in third decade have fine cortical iridescent opacities, which evolve into visually disabling stellate posterior subcapsular cataract by the fifth decade.

## **c) Atopic dermatitis**

About 10% of patients with severe atopic dermatitis develop cataracts in the second to fourth decades. The opacities are often bilateral and may mature quickly. Shield – like anterior subcapsular plaque which wrinkles the anterior capsule is characteristic. Posterior subcapsular opacities resembling a complicated cataract may also occur.

## **3. Traumatic cataract**

Trauma is the major risk factor for unilateral cataract in individuals. The following risk factors are involved in traumatic cataract,

- a) Direct penetrating injury to the lens.
- b) Concussion may cause an imprinting of iris colour on the anterior lens capsule (Vossius ring) as flower shaped cortical opacities (rosette cataract).
- c) Electric shock and lightning are rare causes.
- d) Ionizing radiation.
- e) Infrared radiation- In glassblowers, the IR rays causes exfoliation of the lens capsule which results in thickening of the superficial portion of the capsule and it further splits the deeper layer and protrudes into the anterior chamber.

## **B. Drug – induced cataract**

a) Steroidal drugs may induce cataract. Initially the lens opacities formed in posterior subcapsular region spreads into the anterior region. The relation between dose, duration of administration and the cataract development is unclear. It is understood that children may be more at risk to the cataractogenic effects of systemic steroids and genetic susceptibility may also be of significance. Patients who develop lens physiological changes should have their dose decreased to a minimum, reliable with control of the underlying disease, and if feasible be considered for alternate drug therapy. Premature opacities may regress if therapy is discontinued, alternatively progression may occur despite withdrawn and warrant surgical intervention.

b) Chlorpromazine may cause the deposit of innocuous fine, stellate, yellowish - brown granules on the anterior lens capsule within the papillary area. The deposition of granular material may accumulate on the corneal endothelium and deep stroma. Both lenticular and corneal deposits are dose-related and irreversible. In very high doses (> 2400 mg daily), this drug may cause retinotoxicity.

c) Lens opacities may occur due to the irregular use of Busulphan (Myleran) for the treatment of chronic myeloid leukaemia.

d) Amiodarone, used in the treatment of cardiac arrhythmias, causes visually inconsequential anterior subcapsular lens deposits in about 50% of patients on moderate to high doses.

e) Gold used in the treatment of rheumatoid arthritis, causes harmless anterior capsular deposits in about 50% of patients on treatment for more than 3 years.

f) Allopurinol, used in the treatment of hyperuricaemia and chronic gout, increases the risk of cataract formation in elderly patients, if the cumulative dose exceeds 400 g or duration of administration exceeds 3 years.

### **C. Secondary cataract**

A secondary (complicated) cataract grows as a result of some other primary ocular diseases.

i. Chronic anterior uveitis is the main cause of secondary cataract. The earliest finding is a polychromatic lustre at the posterior pole of the lens which may not progress if the uveitis is arrested. If the inflammation persists, posterior and anterior opacities developed may progress to maturity.

ii. Acute congestive angle closure glaucoma may cause small grey white anterior, subcapsular or capsular opacities within the papillary area.

a. Myopia (Pathological) is linked with posterior subcapsular lens opacities and early-onset nuclear sclerosis, which may ironically increase the myopic refractive error. Simple myopia, however, is not associated with such cataract formation.

b. Hereditary dystrophies such as retinitis pigmentosa, gyrate atrophy, leper congenital amaurosis and stickler syndrome may be associated with posterior subcapsular lens opacities. Cataract surgery may occasionally



improve visual acuity even in the presence of severe retinal changes (Kanski et al., 2003).

## **Free radicals involved in cataractogenesis**

Free radicals may be formed either by the reduction of molecules by electron transfer or by the haemolytic cleavage of covalent bond. Both these reactions may be enzymatic or non-enzymatic.

Due to the presence of an odd unpaired electron in its outermost orbital, these free radicals are unstable and readily react with neighbourhood molecules and extract electrons from them, converting the attacked molecule into a free radical, which in turn attacks another molecule generating more free radicals and so on. This enables free radicals to induce chain reactions that may be thousands of events long. A free radical reaction is terminated by reaction between two free radicals or neutralization by antioxidants (Uday et al., 1999).

## **Fig. 5 Pathways of ROS formation**

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### **Generation of free radicals**

Biological free radicals include reactive oxygen species, reactive nitrogen species, reactive sulphur species, free radicals obtained from xenobiotics.

#### **a) Superoxide anion radical (O<sub>2</sub><sup>-</sup>)**

It is generated from NADPH oxidase and from mitochondria.

i) NADPH oxidase is present in the lysosomal cell membranes. It steals electron from O<sub>2</sub> resulting in the formation superoxide anion radical (O<sub>2</sub><sup>-</sup>). It

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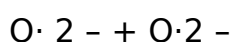
is converted to hydrogen peroxide and is a spontaneous reaction which is known as respiratory burst. This hydrogen peroxide may react with the chlorine in the presence of myeloperoxidase to form hypochlorous acid or it may produce hydroxyl radicals, by the Fenton reaction which uses the metal ion  $Fe^{3+}$ .

ii) From Mitochondria: Ubiquinone, which is a terminal acceptor of electron, is converted to semiquinone (free radical). By reacting with  $O_2$ , it forms ( $O_2^-$ ) super oxide radical with  $H_2O_2$ , it produce hydroxyl radical ion.

## **b) Hydrogen Peroxide**

$H_2O_2$

SOD It is formed by the dismutation of superoxide by the enzyme superoxide dismutase.



Hydrogen peroxide is generated from

i) Aminoacid oxidases: Flavin is a co-enzyme required for the oxidative deamination of amino acid. The reduced flavin attacks molecular oxygen to form hydrogen peroxide.

ii) Xanthine oxidase: Xanthine oxidase catalyses the conversion of hypoxanthine to xanthine and hydrogen peroxide is released from molecular oxygen.

iii) Peroxisomes: Peroxisomes is the site of  $\beta$ - $\xi$ -oxidation of fatty acids.  $\beta$ - $\xi$ -Oxidation of the fatty acids is catalysed by acetyl co-enzyme-A

dehydrogenase. During this process, a co-enzyme called FAD which donates two electrons gets reduced to FADH<sub>2</sub>. Again it is converted to FAD. During that process it gives out O<sub>2</sub> and H<sub>2</sub>O (Kovaceva et al., 2007).

### **c) Hydroperoxyl radical**

They are highly lipophilic and capable of initiating lipid peroxidation.

### **Lipid peroxidation**

Lipid peroxidation is a self-perpetuating common process and involves the conversion of lipid components from cell organelles into lipid peroxides resulting in the formation of a pigment known as lipofuscin. Lysosomal reactive oxygen species are formed as a result of complex oxidative chain reactions in mitochondria during energy production. H<sub>2</sub>O<sub>2</sub> formed in smaller amounts by mitochondria pass through walls of lysosome and react with Fe (II) in a reaction known as Fenton reaction to form potent hydroxyl radicals which cause lipid peroxidation (Halliwell, 2001). Malondialdehyde is the major reactive aldehyde resulting from the peroxidation of biological membrane polyunsaturated fatty acids (PUFA). MDA, a secondary product of LPO, is used as an indicator of tissue damage by a series of chain reactions. MDA is a by-product of prostaglandin biosynthesis. It reacts with thiobarbituric acid and produces a red-coloured product. MDA is a mutagenic and genotoxic agent that may contribute to development of human cancer.

### **Ca<sup>2+</sup> ATPase**

The Ca<sup>2+</sup> ATPase is a transport protein in the cells that serves to eliminate calcium (Ca<sup>2+</sup>) from the cell. It is essential for maintaining the amount of Ca<sup>2+</sup> within the cells. Based upon the electrochemical gradient calcium ion

enter into the cells through the trans membrane. This process is important for the cell signalling by which it lowers calcium level. Thus it is necessary for the cell to utilize ion pumps to remove the  $\text{Ca}^{2+}$ . The  $\text{Ca}^{2+}$  ATPase is expressed in a variety of tissues, together with the brain (Hightower et al., 1982).

## **IN VIVO MODELS IN CATARACT (Gupta, 2004)**

### **1. Sugar cataract**

#### **i) Galactose – induced cataract**

The changes associated with galactose cataractogenesis include the initial reduction of galactose into dulcitol through intervention of aldose reductase with NADPH as a co-factor. Accumulation of dulcitol in the lens, (since it is not metabolized) creates cellular hypertonicity associated with and/or followed by a cascade of events, which includes an influx of water, swelling of the lens fibres, epithelial cell edema, damage of plasma membrane, compromise of cellular permeability, a drop in myoinositol level, a reduction in  $\text{Na}^+$   $\text{K}^+$  ATPase activity an influx of  $\text{Na}^+$  and  $\text{Cl}^-$  and an efflux of  $\text{K}^+$  and the loss of glutathione and aminoacids. These are the morphological, biochemical, enzymatic and molecular alterations in the lens associated with galactose cataracts.

#### **ii) Alloxan – induced cataract**

Alloxan is a cyclic urea analog which is highly reactive molecule that is readily reduced to dialuric acid, which is then auto oxidized back to alloxan resulting in the formation of hydroxyl radical,  $\text{O}_2^-$ , including  $\text{H}_2\text{O}_2$  (hydrogen peroxide). However, the other mechanism reveals the ability of alloxan to

react with protein sulfhydryl groups on hexokinase, a signal recognition enzyme in the pancreatic  $\beta$ -cells that couples changes in the blood glucose concentration to the rate of insulin secretion. By this mechanism, inhibition of glucokinase and other SH containing membrane proteins on the  $\beta$ -cells would eventually result in cell necrosis within minutes.

### **iii) Streptozocin – induced cataract**

Diabetes related cataractogenic changes are seen in the animals injected with streptozocin. This streptozocin initiates cytotoxic action in pancreatic  $\beta$  cells because streptozocin contains a glucose molecule and a highly reactive nitrosourea side chain. It binds to the membrane receptor to generate structural damage. At the intracellular level three major phenomena are responsible for  $\beta$  cell death,

i) Methylation

ii) Free radical production

iii) Formation of Nitric oxide (NO).

The damage caused to  $\beta$  cells alters the sugar metabolism leading to diabetes.

## **2. Selenite – induced cataract**

Selenite cataract resembles human cataract in many ways such as insoluble protein, vesicle formation, increased calcium, reduced glutathione (GSH) and decreased water-soluble proteins. However, selenite cataract shows no high molecular weight protein aggregation or increased disulfide formation and is

dominated by rapid calpain-induced proteolytic precipitation, while senile cataracts may be produced by prolonged oxidative stress.

### **3. Naphthalene – induced cataract**

Naphthalene is oxidized in the liver initially to an epoxide and then it converted into naphthalene dihydrodiol. This stable component is converted enzymatically into dihydroxynaphthalene to reaching the eye. Being unstable at physiological pH, 1, 2- dihydroxynaphthalene and spontaneously autooxidises to 1, 2- naphthoquinone and H<sub>2</sub>O<sub>2</sub>. It alkylates proteins, glutathione and aminoacids and generates free radicals.

### **4. Glucocorticoid – induced cataract**

Glucocorticoid cataract results in the formation of steroid- adduct protein, induction of transglutaminase and reduction of ATPase activity may lead to cataract. Steroid cataracts are produced by the activities of glucocorticoids and progressed by way of production of oxidative stress similar to other types of cataract.

### **5. L- Buthionine – S, R- Sulfoximine (BSO) – induced cataract**

Glutathione is present in mammalian lens in high concentrations and is involved in the protection of lens against oxidation. In most of the cataracts the decrease in its level is observed.

### **6. Smoke – induced cataract**

Cigarette smoke contains trace and heavy metals. The increased metal contents in lens cause lens damage by the mechanism of oxidative stress-

forming oxygen radicals, via metal catalyzed Fenton Reaction. In other words cigarette smoke is associated with the accumulation of iron and calcium.

## **7. UV radiation – induced cataract**

Epidemiological studies have exposed a link between exposure to UV radiation in sunlight and development of cataract. Experimental studies confirm that ultraviolet (UV) radiation induces cataract. There is, however, a lack of data on the age dependence in experimental UV radiation-induced cataract.

## **8. Microwave – induced cataract**

Microwave radiation has been reported to produce posterior subcapsular and cortical cataracts in rabbits and dogs within a short span of time.

## **9. Transforming Growth Factor $\beta$ (TNFB) – induced cataract**

TGFB is induced by injecting approximately 60 ng TGFB into the vitreous. TGFB induce lens epithelial cells to undergo molecular modify and abnormal morphologic that mimic the changes observed in human posterior subcapsular and cortical cataract (Gupta, 2004).

## **IN VITRO MODELS IN CATARACT (Gupta, 2004)**

Induction of cataract in isolated animal lenses maintained in organ culture has become a convenient, quick and appropriate method for testing the anticataract efficacy of an agent. Opacification of lens is induced by generating oxidative stress/ hyperglycemic/ hypergalactosemic conditions around the lens by supplementing the culture medium with a variety of exogenous substances.

## **1. Oxidative stress – induced cataract**

Oxidative mechanisms play an important role in many biological phenomena including cataract formation. Formation of the superoxide radical in the aqueous humor, lens and its derivatization to other potent oxidants may be responsible for initiating various toxic biochemical reactions leading to the progress of cataract. In vitro such cataracts are induced by agents like selenium, H<sub>2</sub>O<sub>2</sub>, photosensitizers and enzyme xanthine oxidase.

## **2. Selenite – induced cataract**

In vitro cataract is produced by supplementing the tissue culture medium with 25 to 100 mM sodium selenite in which freshly enucleated transparent rat lenses are incubated at 37°C. This causes membrane damage and faint cortical opacities within 24 h.

## **3. Photochemically – induced cataract**

Riboflavin, a photosensitizer, is supplemented in the culture medium to induce cataract in cultured lenses. Micro quantities (4-200 μM) of riboflavin lead to severe physiological damage and opacification within 24 h after exposure to light. The initial membrane damage is evidenced by a disturbed cation ratio between lens water and the medium of incubation. Riboflavin on getting photosensitized generates free radicals in a sequence of reactions.

Lenses are maintained in organ culture for 24 to 72 h. The lenses are divided into four groups and incubated in the dark and light both in presence and absence of riboflavin. The lenses are exposed to light with two 15-w daylight fluorescent lamp placed at 8 inches above the cluster plate. The culture medium is replaced every 24 h. Riboflavin shows no effect on the lens in the



absence of light, and light without riboflavin has no significant effect.

opacification starts in the equatorial zone and gradually extends towards the centre of the lens.

#### **4. Enzymatically – induced cataract**

Supplementation of culture medium with 1 mM xanthine and 0.1 unit xanthine oxidase, which act as substrate and enzyme respectively, leads to generation of superoxide radical. The lenses suffer severe oxidative damage and turn opaque within 24 h when incubated in culture medium at 37°C.

#### **5. Hydrogen peroxide – induced cataract**

Incubation of lenses in medium containing 50-500  $\mu$ M H<sub>2</sub>O<sub>2</sub> and it produce cataract. Opacification starts in the equatorial region within 24 h. The entire superficial cortex becomes opaque by 96 h. Due to the high instability of H<sub>2</sub>O<sub>2</sub>, the medium is changed every 2 h during the first eight hours.

#### **6. Sugar – induced cataract**

Transparent and undamaged lenses are incubated in a basic culture medium with fetal calf serum for 24 to 48 h. In the control group the medium is supplemented with glucose (30 mM), lenses develop opacity in the subcapsular region on day 1 and in the central region on day 2. Biochemical analyses reveal raised polyol, malondialdehyde levels and water content, and decreased glutathione levels in these lenses.

#### **7. Steroid – induced cataract**

Steroid-induced experimental cataract is produced in vitro by incubating the transparent lenses in the medium containing methyl prednisolone (1.5 mg/ml). The test agent and methyl prednisolone added alone and together  
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to the medium form drug control, control and treated groups respectively. Early cataract around the equator is produced within 24 h of incubation. Incubation period may be extended to 48 h for dense opacity. Morphological changes and modulation in biochemical parameters between the groups may show the potential of the anticataract agent.

## **8. Naphthalene – induced cataract**

TC-199 medium is used for the preincubation of lens. Stock solution of naphthalene dihydrodiol is prepared in 20% ethanol at  $2.5 \times 10^{-3}$  M concentration. The stock solution is diluted 1: 100 to obtain the final concentration of  $2.5 \times 10^{-5}$  M. The final osmolarity of the solution is 295-300 m Osmol. Rat lenses are incubated in TC-199 medium containing naphthalene metabolite solution. Medium is renewed daily till 72 h. Lenses remain clear during the initial 24 h but from shell-like opacity around the nucleus by 48 h. Opacification becomes more peripheral and widespread after 72 h. At 48 h, under such conditions of incubation, development of opacity mimics the in vivo naphthalene cataract. Naphthalene is oxidized in the liver first to an epoxide and then is altered into naphthalene dihydrodiol. This stable component on reaching the eye gets converted enzymatically to dihydroxynaphthalene. Being unstable at physiological pH, 1, 2 dihydroxynaphthalene spontaneously auto oxidises to 1, 2 naphthoquinone and  $H_2O_2$ . It alkylates proteins glutathione and amino acids and generates free radicals. There is a loss of protein thiol in this reaction and the products are less easily digestible by pancreatin than normal lens protein (Rees and Pirie, 1967).

## 9. Ca<sup>2+</sup> – induced cataract

In this model, the control group contains the lenses incubated in the medium enriched with 20 mM Ca<sup>2+</sup> or 1x 10<sup>-2</sup> mM A23187 calcium ionopore. The treatment group lenses are cultured in the calcium and the test drug-containing medium. Incubation period can range from 24-72 h (Gupta, 2004).

### Fig. 6 Mechanism of action of glucose-induced cataract

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Under physiological conditions, glucose is metabolized through the glycolytic pathway. An excess amount of glucose is converted to sorbitol by enzyme aldose reductase via polyol pathway. The glucose conversion into sorbitol by utilizing NADPH results in the reduction of NADPH/NADP<sup>+</sup>. Moreover, sorbitol undergoes oxidation to fructose by using sorbitol dehydrogenase (SD).

Sorbitol does not easily cross cell membrane. Intra lenticular accumulation of sorbitol, leads to lens damage (Kyselova, 2004).

### Fig. 7 Biomorphological changes during cataract formation

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As, the lens starts to swell in response to the hyper osmotic effects of polyol accumulation, membrane permeability changes resulting in an increase in lenticular sodium and decrease in the levels of lenticular potassium, reduced glutathione, ATP and free amino acids. The overall antioxidant status of the lens decreases because of depletion of GSH (Kyselova, 2004).

## **Mechanism of action of calcium-induced cataract**

### **Fig. 8 Calcium transport pathway**

Increased levels of lenticular calcium activate calcium dependent proteases. The activated proteases hydrolyze cytoskeletal proteins and lens crystalline. Crystalline cleavage would result from lower molecular weight peptides that could, in turn, aggregate to form higher molecular weight proteins (Wang et al., 1996).

### **Various methods for the prevention of cataract**

The development of newer drugs for treatment of cataract mainly aims, interacting at the level of changed lens metabolism and lens pathophysiology. The in vitro, in vivo studies are used to identify the anti cataract agents. This epidemiological studies may be widely classified in the following categories (Gupta et al., 1997).

Aldose reductase inhibitors

Agents acting on glutathione

Nonsteroidal anti -inflammatory drugs

Vitamins, minerals and antioxidants

Miscellaneous agents.

#### **1) Aldose Reductase Inhibitors**

These drugs are aimed to prevent the metabolic dysfunctions of diabetes by polyol pathways. Aldose reductase inhibitors prevents the accumulation of sorbitol within the lens would have an osmotic effect bringing in water and

causing swelling and opacification. Sorbinil a spirohydantoin became the most powerful sorbitol lowering agent. Sorbinil prevents increased fluorescence and protein aggregation and it also acts as an antioxidant.

## **2) Non Steroidal Anti inflammatory Drugs**

The NSAIDS broadly studied are paracetamol, aspirin, Ibuprofen, sulindac, naproxen, and bendazec. The NSAIDS provide adequate productive effect to lens protein through various steps like acylation, carbamylation and inhibition of glycosylation. Some of them are also reported to inhibit lens AR to varying extent. NSAIDS contains antioxidant properties also. Most of the studies on the evaluation of anticataract potential of drugs have been conducted by feeding the drugs by oral route.

## **3) Agents which act on glutathione**

Glutathione is a tripeptide thiol known to control calcium influx and protect lens protein from various agents like glucose and galactose. With advancing of age there is a considerable decrease in the concentration of glutathione and the decrease more prominent in lens with cataract.

## **4) Vitamins, minerals and antioxidants**

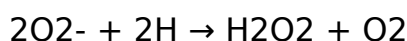
If oxidation in lens leads to cataract formation, then is feasible to prevent it by the use of antioxidants such as vitamins C and E and perhaps  $\beta$ -carotene. The potential role of vitamins and antioxidants in preventing various diseases is well documented there are reports suggesting beneficial effect of vitamins like C and E in preventing cataract. Beta -carotene has also been demonstrated to protect lens damage by hematoporphysin. Ascorbate protects rubidium uptake against free radical damage and prevents light

induced protein cross linking. Protective effect of vitamin C has been also reported in various in vitro studies. Vitamin E has been found to delay cataractogenesis in diabetic rats and in Emory mouse. Vitamins C and E,  $\beta$ -Carotene and other anticataract agents probably act via a common mechanism of their scavenging properties of free radicals (Gupta et al., 1997b).

## **Antioxidant enzymes**

### **1) Superoxide Dismutase (SOD)**

SODs are a family of metalloenzymes that transfer superoxide into hydrogen peroxide ( $H_2O_2$ ) and represents the first line of defence against oxygen toxicity.



Three isoforms of SOD have been found. The first is mainly found in the cytoplasm of cells and it containing Cu and Zn at its active site (Cu/Zn SOD-1), the second containing Mn at its active site is located in mitochondria (Mn SOD-2) and the third (Cu/Zn SOD-3) is present in the extracellular fluid like plasma. SOD is a stress protein which is synthesized mostly in response to oxidative stress. It is found that little amount of Cu, Zn and Mn metals are crucial for maintaining the antioxidant activity of SOD (Halliwell, 1994; Ray and Husain, 2002).

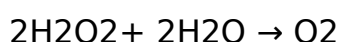
### **2) Glutathione Peroxidase (GPx)**

GPx is one of the most important enzymes responsible for the degradation of organic peroxides and hydrogen peroxide in the brain. GPx catalyse the oxidation of GSH to GSSG at the expense of  $H_2O_2$ . There are two isoforms  
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have been identified, selenium-dependent which is highly active towards H<sub>2</sub>O<sub>2</sub> and organic hydroperoxides and selenium independent GPx. GPx activity has been reduced in selenium deficiency (Muller et al., 1984; Son et al., 2007).

### **3) Catalase (CAT)**

It is a heme-containing protein present in most cells.



Catalase is 10<sup>4</sup> times faster than GPx. It is having four protein subunits, each containing a heme Fe (III)-protoporphyrin group bound to its active site. GPx and CAT were found to be important in the inactivation of many environmental mutagens (Ray and Husain, 2002).

### **4) Glutathione (GSH)**

GSH has major intracellular antioxidant molecule and it is a tripeptide synthesised by enzymatic reaction involving two molecules of ATP from aminoacids like glutamate, glycine and cysteine. It plays a very crucial role in detoxification of peroxides and electrophilic toxins, mainly by acting as a substrate for GSH transferase and GSH peroxidase. It was shown that weakening of GSH enhances cerebral ischemic injury in rats (Mizui et al., 1992; Son et al., 2007).