INTRODUCTION AND REVIEW
The eye enables animals to perceive the world by converting light into electrical signals. It is also a window through which the working of the brain can be discerned. Eye has a crystallin lens positioned behind the iris which refracts the light entering the eye through the pupil and focuses it on the photosensitive retina. The main functions of the lens are to provide refraction of light, accommodation and absorption of ultraviolet light (Cotlier, 1989).

The mammalian crystallin lens is transparent, avascular, flexible, resilient and biconvex in nature (Cotlier, 1989). The lens is covered with mucopolysaccharide capsule produced by epithelial cells. The epithelial cells divide near the lens equator. The cells elongate towards poles and become lens fibre, which comprises the bulk of lens mass. As the lens matures the oldest cells of the fibre lose their nuclei and mitochondria. Such cells get compressed in the centre and form the nucleus of the lens. Later on, new fibre cells overlay the nucleus resulting in the formation of cortical fibre (Hogan, Alvarado and Weddell, 1971).
Lens is a dehydrated organ and contains approximately 66% water and 33% protein. The remaining 1% solid comprises of carbohydrates, lactic acid, glutathione, amino acids, ascorbic acids, lipids, ions, etc. The cortex of the lens is less dehydrated than the nucleus, which is maintained by an active Na$^+$ ion-water pump that resides within the membranes of cells in the lens epithelium and each lens fibre.

The protein content of the lens is higher than that of any other organ in the body and is organ specific. The perfect physicochemical arrangement of the lens proteins gives transparency to the lens (Delaye and Tardieu, 1981). The normal human lens contains two major protein fractions i.e., (a) soluble proteins (crystallin) which comprises 85% of the total lens protein. These crystallins are further subdivided into α-crystallin (15%), β-crystallin (55%) and γ-crystallin (15%), (b) insoluble protein (albuminoid) which constitutes remaining 15% of total lens proteins (Harding and Dilley, 1976: Fu, Wagner and Hart, 1984). The major share of the insoluble proteins is found in the nucleus of the lens while the soluble proteins are in the lens cortex (Harding and Dilley, 1976).

The lens and the red blood cells have certain structural similarities like loss of nuclei and mitochondria. Both utilize glucose as major energy source.
Normal and early stages of lens and erythrocyte is wellmaintained by the different physiological mechanisms. As the age advances, the normal functional status of lens deteriorates. Similar changes are not observed in case of erythrocytes, since they are renewed periodically. The structural and functional changes in the lens may give rise to cataract.

Cataract is defined as alterations in the optical homogeneity of the lens or decrease in its transparency. It can also be defined in terms of abnormal morphology or biochemistry, decreased light transmission, optical aberrations, decreased visual acuity or in terms of all of these parameters. Abnormal morphology includes vacuoles, water clefts, dense areas reflecting or refracting light and punctuating microscopic dots (Cotlier, 1989). In simple terms any opacity in the lens whether it is localised or involving the entire lens is called cataract (Bhat, 1993).

The type of cataract which appears usually after the age of 30 to 40 years progress further which ultimately results in severe visual impairment is called senile cataract (Balasubramanian, Bhat and Rao, 1990). It has long been known that cataract occurs predominantly in older people. Hence the term called senile cataract (Hockwin, 1985). In other words, any cataract that
develops in elderly people generally over 60 years of age, without a known cause is called senile cataract (Myron and Ben, 1982) and is about 85% of all known cataract (Adler, 1981). It is the most common cause of visual incapability and blindness, which reflects the state of senescence. It occurs in 65% of people in the age groups of 60-65 years and 95% of the people above 65 years of age. Duke-Elder (1969) and Weale (1982) were of the opinion that in majority of the cases the progress of cataract is slow (Table 1).

Table 1. Incidence of cataract in various age groups

<table>
<thead>
<tr>
<th>Reference</th>
<th>41-50 (%)</th>
<th>51-60 (%)</th>
<th>61-70 (%)</th>
<th>Above 70 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anderson (1924)</td>
<td>38.2</td>
<td>65.1</td>
<td>85.0</td>
<td>92.0</td>
</tr>
<tr>
<td>Gradle (1926)</td>
<td>34.1</td>
<td>66.2</td>
<td>68.4</td>
<td>90.9</td>
</tr>
<tr>
<td>Cinotti and Patti (1968)</td>
<td>63.3</td>
<td>58.2</td>
<td>83.2</td>
<td>93.1</td>
</tr>
</tbody>
</table>

(Duke-Elder, 1969)

Cataract is the main cause of visual incapability and blindness all over the world (Balasubramanian et al., 1990). There are about 27-35 million blind people in the world (Foster, 1991). Out of these, 17 million are blind by cataract (Kupfer, 1984). In a developing country like
India, cataract contributes greatly to blindness. More than 50% of the 9-12 million blind people in the country have surgically curable cataract (Minassian and Mehra, 1990).

The main causes for visual impairment and blindness in India are:

- Cataract - 55%
- Trachoma and infections - 20%
- Malnutrition - 20%
- Injuries - 1.2%
- Glaucoma - 0.5%
- Others - 3.3%

Siva Reddy (1989) observed that 55% of visual incapability in India is curable and 42% is preventable, i.e., 92% of blindness in India is avoidable. The blindness due to cataract can be treated successfully with modern medical technology. The rate of development of cataract is much more in India in comparison with other countries (WHO, 1984).

About 1.5 million new cases of blindness due to cataract are reported every year in India (WHO, 1984). Prevention of cataract or delaying its progress would be a major achievement in human welfare. If one can manage to delay the development of cataract by 10 years, the number
of cataract operations would get reduced to nearly one half (Kupfer, 1984). Given below is the percentage of cataract in different countries.

Table 2 Percentage of cataract in different countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Percentage</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Britain</td>
<td>22.60</td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>15.65</td>
<td></td>
</tr>
<tr>
<td>Kenya</td>
<td>45.00</td>
<td></td>
</tr>
</tbody>
</table>

Senile cataract is becoming more frequent worldwide since the life span of the population increases and majority of cases occur in older age groups (Bhat, 1993). The percentage of senile cataract in different age groups in United States are given below (Table 3).

Table 3 Percentage of senile cataract in different age groups in United States

<table>
<thead>
<tr>
<th>Country</th>
<th>Age group</th>
<th>Percentage</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>52-64</td>
<td>5.0</td>
<td>Khan, Leibowitz, Ganley, Kini and Cotton (1977)</td>
</tr>
<tr>
<td></td>
<td>65-74</td>
<td>18.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>75-85</td>
<td>46.0</td>
<td></td>
</tr>
</tbody>
</table>
The percentage of senile cataract in certain parts of India is given in Table 4.

Table 4  Percentage of senile cataract in different states of India

<table>
<thead>
<tr>
<th>State</th>
<th>Age groups (Years)</th>
<th>Percentage</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Punjab</td>
<td>Over 30</td>
<td>13.00</td>
<td>Franken and Mehta (1968) and Chatterjee (1973)</td>
</tr>
<tr>
<td>Haryana</td>
<td>Over 30</td>
<td>13.00</td>
<td></td>
</tr>
<tr>
<td>Western UP</td>
<td>40-50</td>
<td>15.91</td>
<td>Raizada, Mathur and Narang (1984)</td>
</tr>
<tr>
<td>Punjab</td>
<td>40-50</td>
<td>2.20</td>
<td>Chatterjee et al. (1982)</td>
</tr>
<tr>
<td>Punjab</td>
<td>Over 60</td>
<td>31.00</td>
<td>Franken and Mehta (1968) and Chatterjee (1973)</td>
</tr>
<tr>
<td>Haryana</td>
<td>Over 60</td>
<td>31.00</td>
<td></td>
</tr>
<tr>
<td>Punjab</td>
<td>Above 70</td>
<td>87.80</td>
<td>Chatterjee et al. (1982)</td>
</tr>
<tr>
<td>Western UP</td>
<td>Above 80</td>
<td>86.95</td>
<td>Raizada et al. (1984)</td>
</tr>
</tbody>
</table>

There exists a difference of opinion about the percentage incidence of cataract between sexes. Chatterjee et al. (1982) reported that the percentage of cataract in men and women as 16.9 and 13.7%, respectively. Raizada et al. (1984) found the percentage as 8.4 in men and 11.09 in women.
A number of factors are responsible for the formation of cataracts in old age as shown in Figure 1.

Figure 1 Diagrammatic representation of the interplay of age and various risk factors in the formation of lens opacities.
The risk factors can produce alteration in the structure of lens resulting in loss of transparency (Bunce, 1980; Hockwin, 1985; Chylack, 1984; Raizada et al., 1984).

The risk factors listed by National Advisory Eye Council (1983) are as follows:

1. Ultraviolet light
   a. Sunlight
   b. Occupational exposure
2. Ionizing radiation
3. Radio frequency and microwave radiation
4. Toxic drugs and chemicals
5. Diabetes
6. Elevated blood pressure
7. Family history
8. Biochemical agents
   a. Galactokinase deficiency
   b. Elevated plasma tryptophan levels
   c. Glucose 6-phosphate dehydrogenase deficiency
   d. Proteins and lipids

Harding and Crabbe (1984) is of the opinion that physical, mechanical or chemical insult can induce cataract. Various agents such as trauma, chemicals, radiation, electricity, viruses, vitamins and deficiency of amino acid can trigger cataractogenesis in man
Cataract may be associated with diseases of skin, central nervous system, skeletal system, chromosomal abnormalities and other ocular diseases or malformation (Cotlier, 1989). Chylack (1984) is of the opinion that age, corticosteroid, radiation and diabetes may accelerate the rate of cataractogenesis. O'Brien and Malsberry (1934), Clayton, Cuthbert, Seth, Phillips, Bartholomew and Reid (1984) considered high blood glucose level and diabetes mellitus as risk factors. Electromagnetic radiation such as microwave and infrared radiation is also considered as a causative factor (Lerman, 1980). Exposure to ultraviolet rays, i.e., B-radiation (295-320 nm) especially in countries with hot climates have been considered as risk factor (Duke-Elder, 1926; Clayton et al., 1984; Hiller, Sperduto and Ederer, 1986; Taylor, West and Rosenthal, 1988; Balasubramanian et al., 1990; Bhat, 1993). Chatterjee (1973) and Balasubramanian et al. (1993) observed low cloud as one of the causative factors. A critical role of pollutants, pesticides, cigarette smoke and burning of cheap cooking fuel results in the formation of cataract (Duncan, 1981; Clayton, Cuthbert, Duffey, Seth, Phillips, Bartholomew and Reid, 1982; Klein, Klein and Moss, 1985; Sheila, Beatriz, Edward, Hugh and Taylor, 1989; Balasubramanian et al., 1990; Bhat, 1993). Duncan (1981) and Balasubramanian et al. (1990) reported that cataract
can also form as a result of trauma, inflammation, metabolic or nutritional deficiency.

Nutritional deficiency or malnutrition especially, deficiency of protein may bring about cataract (Duke-Elder, 1969; Bhat and Gopalan, 1974; Bunce, Hess and Fillnow, 1978; Rawal, Patel and Desai, 1978; Daljitsingh, Kumar, Verma and Mohinder, 1979; Sing, 1980; Adler, 1981; Cotlier, Sharma, Zucherman, Pucklin, Teasley and Irvine, 1981; Skalka and Prchal, 1981; Bhat, 1982; Gupta, Gupta and Pahda, 1982; Libondi, Rinaldi and Miele, 1983; Bhat, 1987; Jacques, Hartz, Chylack, MacGandy and Sadowsky, 1988; Balasubramanian et al., 1990). The gastrointestinal infection results in diarrhoea which in turn result in malnutrition, acidaemia, uraemia and renal failure may enhance the formation of cataract (Harding and Rixon, 1980; Chatterjee et al., 1982; Minassian, Mehra and Jones, 1984). Methyl isocyanate can also damage the eyes especially the lens as in the case of Bhopal gas tragedy resulting in the formation of cataract (Project Advisory Committee Report of ICMR, 1989).

High mineral intake and heavy consumption of yoghurt can induce cataract (Chatterjee et al., 1982). This could lead to chronic accumulation of metal ions such as Ca²⁺ in the lens. Abnormal levels of Ca²⁺ lead to lenticular opacity (Lorand, Conard and Velasco, 1985) by altering the
membrane permeability and other cumulative changes in crystallin.

Sprinker, Harr, Newbene, Whanger and Weswig (1971), Swanson and Truesdale (1971), Lawrence, Sunde, Schwartz and Hockstra (1974), and Whanger and Weswig (1975) have reported the role of selenium in the formation of cataract whereas Sprinker et al. (1971), Whanger and Weswig (1975), Ketola (1979) and Bhat (1988) suggested the role of zinc in the development of cataract. Bhat (1988) proposed that copper can also induce cataract formation.

Association between alcohol consumption and cataract has been suggested by Clayton et al. (1982). The role of increased blood pressure in cataractogenesis has been highlighted by Khan et al. (1977) and Hiller et al. (1986). Hockwin (1985) is of the opinion that tranquillizers, hypertension medication and diuretics can bring about cataract. But Chen, Zen, Ma, Su and Mao (1992) proposed genetic factor for cataractogenesis.

Rinaldi, Albini, Costagliola, De-Rosa and Auricchio (1984) observed that formation of cataract can also result from a defect in the metabolism of lactose. The risk of cataract appears to be increased with lower levels of antioxidants viz., glutathione peroxidase and glucose 6-phosphate dehydrogenase (Balasubramanian et al., 1990).
Cataracts may be classified as under:

(1) **Developmental cataracts:** In which the normal development of the lens fibres and epithelium has been affected during growth by hereditary, nutritional or inflammatory changes with consequent loss of transparency.

This group includes the congenital forms of anterior and posterior polar cataracts, central cataract, zonular cataract, coronary and punctate cataracts and complete congenital and juvenile cataracts.

(2) **Degenerative cataracts:** In which the lens loses its transparency as a result of degenerative changes due to various causes. This includes senile nuclear and cortical cataracts, radiation cataracts, lightening, electric and heat ray cataracts, complicated cataracts, cataract associated with systemic diseases or poisoning and traumatic cataracts (James Allen, 1963). Cataracts can be grouped anatomically according to the part of the lens involved, into anterior or posterior subcapsular, cortical or nuclear (James Allen, 1963; Phelps, 1986; and Lentz, 1986). They can also be divided into progressive and stationary cataracts or hard, soft and fluid cataracts; or partial or complete cataracts (James Allen, 1963).

Senile cataract is quite common at the age of fifty and above but occasionally it is seen as early as 40s.
Almost always both the eyes are involved but generally one in advance to the other. The opacity may begin either superficially in the cortex (cortical) or immediately surrounding the nucleus (nuclear) (James Allen, 1963).

The nucleus or the centre is usually the first place to become opaque in the aging eye (Bhat, 1993). The maximum incidence of cataract is between the age of 50-70 years for cortical and 70-75 years for nuclear cataract (Duke-Elder, 1969). The time required for full development of cataract varies from few months to many years. The different stages of senile cataract are as follows.

1. **Incipient stage**: The opacity begins as streaks which extends from the periphery of the cortex to the centre of the lens. The streaks are wider in the periphery and narrow in the centre. This stage is referred to as presenile stage. Cataract often remains stationary in the incipient stage with little or no impairment of vision or it may pass on to the next stage.

2. **Intumescent stage**: During this stage the lens imbibe fluid and swells up which results in the loss of transparency. There is also transformation of colour from transparent to shiny bluish white colour and lens also possesses distinct markings of stellate figure. Such a
stage is called as immature stage of senile cataract (James Allen, 1963). Immature cataract posses vacuoles in the lens cortex and small opacities in the cortex or with changes in colour and opacities in the nucleus (Cotlier, 1989). Certain cases of senile cataracts, especially the nuclear sclerosis type do not pass through the intumescent stage but directly pass on to the mature stage.

3. **Mature stage:** The lens loses its excess fluid, shrinks somewhat and becomes perfectly opaque and posses a dull gray or amber colour and shows the visible stellate markings (James Allen, 1963). Therefore mature cataract can be defined as that stage of cataract in which the lens becomes completely opaque and white in colour (Cotlier, 1989).

Duke-Elder (1969) observed certain changes in the colour of the lens to dark brown and along with these colour changes, the lens becomes completely opaque which is referred to as "cataracta brunescence". This can transform into black cataract which is otherwise called as hard cataract. This is because of the intensification of physiological changes of sclerosis in nucleus (Dilley and Pirie, 1974). The change in colour from dull gray, yellow, dark yellow, yellow brown, amber brown, reddish brown and finally to black is due to deposition of melanin. These stages of colour change are also called
"cataracta nigra" or "cataracta brunescence" (James Allen, 1963; and Duke-Elder, 1969). The transformation of colour and hardening of nucleus is parallel with decrease in transparency (Harding and Crabbe, 1984). Thus nuclear cataracts are of two types. They are (1) Lens with double focus or false cataract, (2) Black cataract. Symptoms of nuclear cataract are initial shift to myopic refraction, mononuclear diplopia or poor hue discrimination. Typically, nuclear cataracts take longer time before they interfere sufficiently with vision to warrant extraction of cataract (Balasubramanian et al., 1990). At the mature stage, cataract can be separated easily from the capsule of the lens.

4. **Hypermature stage:** The cataract may continue in the mature stage for longer time. During this stage the surface of the lens loses its radial markings and becomes homogeneous or presents irregular spots. The lens may continue to lose its water resulting in a dry flattened mass, i.e., "shrunken cataract" or the cortex may become soft (James Allen, 1963; and Duke-Elder, 1969), liquid and milky. The nucleus sinks to the bottom of the fluid giving rise to white colour with brownish markings below (James Allen, 1963). Very old hypermature cataracts often shows the deposits of cholesterol or lime salts which is called as "chalky cataracts". This change is found chiefly in complicated cataracts. The lens may become
tremulous through stretching of the suspensory ligament during hypermature stage. And for these reasons, operation upon hypermature cataract is less favourable and more difficult than mature cataract (James Allen, 1963).

Duke-Elder (1969), and Myran and Ben (1982) classified senile cataract as

1. **Cuniform**: Opacities develop in the peripheral cortex forming radial spikes or riders.
2. **Punctate perinuclear**: Opacities appear in the cortex next to nucleus.
3. **Cupliform**: Opacities develop in the posterior cortex.

The role of various risk factors in the formation of senile cataract cannot be ruled out. Rawal, Khamar and Gandhi (1982) propose that the metabolic changes in the lens during aging might influence the formation of senile cataract. Skalka and Prachal (1980), Cotlier, Sharma, Niver and Brescia (1983), and Hockwin (1985) reported that the intensity of metabolic activity decreases in the lens due to decrease in the available metabolites in old age. This may not be true in the case of erythrocytes, since its life span is limited. Even though they possess similar structural and metabolic activities, it is proved beyond doubt that the sole source of energy in the lens is glucose. In the absence of direct blood supply to the lens, metabolic exchange of glucose occurs through aqueous
humor, whereas in erythrocytes absorption of glucose takes place directly from the circulation.

Due to the low metabolic rate in lens in comparison to other tissues, it has often been termed as bradytrophic tissue (Hockwin, 1985). The glucose present in the lens is either phosphorylated to glucose 6-phosphate or rapidly metabolised through the main pathways viz., the glycolytic pathway, the Kreb's cycle, the hexose monophosphate shunt (HMPS) and the sorbitol pathway (Chylack and Cheng, 1978; and Harding and Crabbe, 1984). The main metabolic activities of the red cells are related to glycolysis and glutathione metabolism (DeGurchy, 1985). The main features of metabolic process in lens is predominantly glycolytic breakdown of carbohydrates, especially glucose (Hockwin, 1985). In the case of erythrocytes, 90 per cent of glucose is metabolised via Embden Meyerhof pathway or glycolytic pathway (DeGurchy 1985). The energy which is released is utilised for the synthesis of glutathione, especially reduced glutathione (GSH), the maintenance of transparency of lens and electrolyte balance, and to a certain extent for the process of accommodation (Kinoshita, 1965 and Hockwin, 1985).

The Kreb's cycle requires oxygen and it is very inactive in lens and erythrocytes since they lack mitochondria and oxidative enzymes. The hexose monophosphate shunt is extremely active in lens and
erythrocytes (Zinkham, 1961; Yoshida, 1973; Harding and Crabbe, 1984; Giblin, McCready, Reddan, Dziedzic and Reddy, 1985). The enzymes involved in this pathway are located in the cytosol. This means that the oxidation is not dependent on mitochondria or the tricarboxylic acid cycle. The primary purpose of hexose monophosphate shunt (HMPS) is to produce NADPH, which is utilised for various biosynthetic reactions in order to maintain lens and erythrocyte glutathione in the reduced state (GSH) (Eggleston and Kreb, 1974; DeGurchy, 1985; Devlin, 1986).

The major enzymes involved in HMP shunt are glucose 6-phosphate dehydrogenase (G6PD) (EC 1.1.1.49), transketolase (TK) (EC 2.2.1.1) and transaldolase (TA) (EC 2.2.1.2). Their functional roles are given in Figure 2. Out of these, G6PD is NADP+ specific, found in almost all the tissues of higher organisms and in most prokaryotes as well (Betke, Beutler, Brewer, Kirkman, Luzzatto, Motulsky, Ramot and Siniscalco, 1967; Beutler, 1983; and Devlin, 1986). The NADPH thus produced is utilised by glutathione system and glutathione linked enzymes. The glutathione system includes reduced glutathione (GSH) and oxidised glutathione (GSSG). The glutathione linked enzymes are glutathione peroxidase (GSH-PO) (EC 1.11.1.9) and glutathione reductase (GSH-R) (EC 1.6.4.2).
GSH-PO - Glutathione peroxidase, GSH- Reduced glutathione, GSH-R - Glutathione reductase, GSSG - Oxidised glutathione, G6-P - Glucose 6-phosphate, G6PD - Glucose 6-P dehydrogenase, F6-P - Fructose 6-P, TA - transaldolase, 6PGD - 6-Phosphogluconate dehydrogenase, TK - transketolase; GA-3P - Glyceraldehyde 3-P, PRI - Phosphoribose isomerase, XPE - xylulose phosphate epimerase.

**Figure 2** Interrelationship between HMP shunt, glutathione and glutathione linked enzyme system

The major antioxidant defense system in the human body includes GSSG, GSH, GSH-PO, GSH-R and G6PD (Bando and Obazawa, 1990; Bhat, John, Reddy, Reddy and Reddy, 1991). The interrelationship between HMP shunt, glutathione and glutathione linked enzyme systems are given in Figure 2.
G6PD, being a key enzyme of the HMP shunt and antioxidant defense system, controls the various enzymatic and physiological characteristics of lens and erythrocytes. G6PD deficiency is considered as a risk factor in cataractogenesis (Hatcher, 1981; Orzalesi, Sorcinelli and Guiso, 1981; and Chen et al., 1992) and hence a change in the activity of this enzyme in lens as well as erythrocytes is expected. In the lens, G6PD takes part in a series of activities that are indispensable for the growth and maintenance of transparency (Hatcher, 1981; Orzalesi et al., 1981; Meloni, Carta, Forteleoni, Carta, Ena and Meloni, 1990; and Chen et al., 1992) and takes part in the defensive mechanism against oxidative stress (Kinoshita, 1964; Ohrloff, Bous and Hockwin, 1976; and Giblin et al., 1985).

In erythrocytes G6PD is essential for the integrity and defence against oxidation, by the help of glutathione system (Kinoshita, 1964; Giblin et al., 1985 and Meloni et al., 1990).

G6PD activity was altered in senile cataract (Beutler, 1959), especially in the cortical region of the lens (Zinkham, 1961). Zinkham (1960, 1961), Westring and Pisciotta (1966), Helge and Broner (1966), Donnel, Bergren and Ng (1967), Orzalesi et al. (1981), Orzalesi, Fossarello, Sorcinelli and Schlich (1984), Moro, Gorgone,
Livolti, Cavallaro, Faro, Curreri and Mollica (1985), Vanella, Gorgone, Cavallaro, Castorina, Campisi, diGiacomo, Bousquet, Livolti and Mollica (1987), Yuregir, Varinli and Donma (1989). Bhat et al. (1991) and Chen et al. (1992) observed G6PD deficiency in the cases of cataract and proposed a relationship between G6PD deficiency and development of cataract. Zinkham (1960) was the first to report a change in activity of G6PD in lens and erythrocytes. This change in activity of G6PD in mature cataract was not as severe as that of immature cataract. Zinkham (1961), Moro et al. (1985), Vanella et al. (1987), Yuregir et al. (1989) and Chen et al. (1992) reported G6PD deficiency both in lens and erythrocytes of patients with cataract. Bhat et al. (1991) found that the specific activity of G6PD was altered during the browning of lens. However, the enzyme activity when expressed per unit weight, was found to be unaltered between brown and yellow lenses. Donnel et al. (1967) pointed out a single case of "zonular cataract" due to G6PD deficiency. But Angra, Munjal and Jaffery (1985), in contrast, failed to notice any significant change in G6PD deficiency in patients with congenital cataract. Helge and Broner (1966), and Westring and Pisciotta (1966) reported cases of cataracts in children with G6PD deficiency.
Absence of positive correlation between G6PD deficiency and cataract was reported by Addis and Vitali (1970), Behera and Devdas (1979), Panich and Na-Nakorn (1980). Bhatia, Patel and Dubey (1990) also did not find any significant difference in G6PD deficiency between cataract cases and control. Orzalesi et al. (1981) and Chen et al. (1992) observed that G6PD deficiency was more frequent in the presenile group (40-60) of cataracts than in the senile group. Orzalesi et al. (1984) and Bhatia et al. (1990) reported that the deficiency rate was much more among 40-50 year group in comparison with older age group or senile group.

In short, the effect of G6PD deficiency is the loss of integrity of erythrocytes and lens. Haemolysis occurs as a result of insult to the erythrocytes, the comparable situation in the lens would be liquifaction of the fibres (Kinoshita, 1964; Rathbun, 1976; Augusteyn, 1979; Moro et al., 1985; Vanella et al., 1987; Meloni et al., 1990; and Chen et al., 1992).

Senile cataract is characterised by multiple risk factors which have already been discussed earlier. The mechanisms that bring about the loss of transparency include oxidation, osmotic stress and chemical modifications (Bunce, Kinoshita and Horwitz, 1990). The etiology of senile cataract is due to oxidative stress as
These mechanisms lead to the formation of noncovalent disulfide protein bonds, mixed disulfide bond formation with glutathione, covalent bond formation, lower molecular weight peptide formation, protein crosslinking, protein modification i.e., loss of solubility, etc. (Dische and Zil, 1951; Barber, 1973; Harding, 1973; Rathbun, 1976; Dillion et al., 1976; Truscott et al., 1977; Truscott and Augusteyn, 1977a, 1977b; Anderson and Spector, 1978; Augusteyn, 1979; Augusteyn, 1984; Chylack, 1984; Harding and Crabbe, 1984; Spector, 1984; Hockwin, 1985; Cotlier, 1989; Kamei, 1990; and Bhat, 1993).

Oxidative mechanism in ocular tissue is brought about by various factors. They are one or more oxidising forms of oxygen viz., superoxide anion (O$_2^-$), hydroxyl radical (OH), molecular oxygen (O$_2$), hydrogen peroxide (H$_2$O$_2$) and free radicals (Pirie, 1972; Fridovich, 1976; Garner and Spector, 1980; Duncan, 1981; Zigman, 1981; Grossweiner, 1984; Bhuyan and Bhuyan, 1983; Chylack, 1984; Bhat, 1991; and Bhat, 1993). The oxidising forms of oxygen is produced in biological system by the reduction of molecular oxygen or oxidation of sugars (Fridovich, 1976; Hunt, Dean and Wolff, 1988).

Molecular oxygen is produced by photochemical reaction or photo-oxidative process and from the hydrogen peroxide present in the aqueous humor (Pirie, 1965;
Hydrogen peroxide can be formed during the oxidation of ascorbic acid (Reddy, 1971), or can also be formed from superoxide anion by the help of superoxide dismutase (Bessens, 1983). It can also be formed as a toxic metabolite of oxygen (Giblin, Chakrapani and Reddy, 1979; Goosey, Zigler and Kinoshita, 1980; Spector and Garner, 1981; Weigard, Jose, Rapp and Anderson, 1984; Tomba, Gandolfi and Maraini, 1985).

Superoxide anion can be formed from free radicals and molecular oxygen by the help of ascorbic acid, or from the H$_2$O$_2$ present in the aqueous humor (Pirie, 1965; Bessens, 1983). Hydroxyl radicals are produced by hydrogen peroxide present in the aqueous humor (Pirie, 1965). Free radicals are highly reactive species containing one or more unpaired lone electrons in the outer orbits. They are generated endogenously inside the cells as a result of normal metabolic processes. They can also be produced extracellularly by factors such as natural radiation, pollutants, pesticides, smoke, especially from cigarette and cheap cooking fuel, etc. (Bhat, 1993). Among the various forms of oxygen, superoxide anion and hydrogen peroxide are seemed to be the most powerful oxidants which are harmful to the lens (Weiter and Sabramanian, 1978; Chylack, 1984).
Osmotic stress occurs as a result of defects in cation transport, oxidation of -SH (sulphydryl) groups of sodium potassium adenosine triphosphatase (Na\(^+\)K\(^+\)ATPase), membrane malfunctions, electrolyte imbalance due to loss of glutathione, alteration in the salt and water balance, etc. (Kinoshita, 1964; Duncan and Bushell, 1975; Fuki, Herola and Kinoshita, 1976; Rathbun, 1976; Spector and Roy, 1978; Duncan and Bushell, 1980; Reddy, Giblin and Matsuda, 1980; Augusteyn, 1981; Rathbun and Bovis, 1986; and Bunce et al., 1990).

Osmotic stress increases the membrane permeability, or accumulation of osmolytes, and the net increase in sodium chloride and water. These imbalances can rupture the membranes of fibre cells. It in turn may promote loss of proteins depending upon the maturity of cataract and aggregation of proteins (Barber, 1968; Augusteyn, 1981; Bunce et al., 1990). When osmotic imbalance occurs, the resultant appearance of vacuoles or clefts brings about changes in refractive index and increased efficiency of light scattering. This is what is observed in mature senile cataract (Barber, 1973; Cotlier, 1989; and Bunce et al., 1990).

In the case of normal lens there is no vacuole or cleft formation. The membrane fibres of the lens and lens capsule do not allow the passage of protein molecules from the lens to the aqueous humor (Cotlier, 1989).
Stevens, Rouzer, Monnier and Cerami (1978), Bloemendal (1981), Liang and Chakrabarti (1981), Spector (1984), and Bunce et al. (1990) noticed chemical modifications as a result of aging. One such chemical modification occur as a result of protein glycosylation, as seen in diabetic cases. It can otherwise be called as glycosyl-lysine modification, which is due to nonenzymatic glycosylation of the epsilon amino group of lysine. This modification thus results in conformational changes in protein, by the formation of S-S bonds through oxidation of adjacent sulphydryl groups, which may result in protein aggregation and ultimately resulting in opacification, which is seen significantly in diabetic cataract (Stevens et al., 1978).

Another chemical modification of lens proteins is carbamylation produced by the addition of cyanate, which occurs secondary to accumulation of metabolites from urea cycle as in uraemia, or secondary to dehydration (Harding, 1980; Beswick and Harding, 1984; Harding and Crabbe, 1984). The net effect of chemical modification is change in conformation and increased susceptibility to oxidation.

In nutshell the effect of oxidation, osmotic effect and chemical modifications are disintegration of plasma membranes of lens fibres, leakage of low molecular weight

Bunce et al. (1990) were of the opinion that the osmotic effects are noticed in lens cortex whereas aggregation of protein occurs primarily in the lens nucleus. Garner and Spector (1982) were of the opinion that oxidation precedes opacification and disulfide linked aggregates would be found primarily in opaque regions.
Indeed, if an examination is made of cataracts which are either essentially nuclear or cortical, extensive oxidation is found in both clear and opaque regions (Garner and Spector, 1980a). But in nuclear cataracts, large protein membrane aggregates are observed only in the nucleus and in cortical cataracts, the HMW disulfide linked aggregates are primarily found in the cortex. This observation supports the concept that oxidation precedes the aggregation process. Oxidation is characterised by aggregation and insolubilisation of lens proteins and is considered as an immediate cause of lens opacity.

Aggregation and insolubilisation of lens proteins can take place in the absence of reduced glutathione, presence of increased GSSG, disturbance in antioxidant system, nutritional deficiency and altered environment (Reddy, 1971; Rathbun, 1976; Spector and Roy, 1978; Augusteyn, 1979; Garner and Spector, 1979; Augusteyn, 1981; Augusteyn, 1984; Reddy and Giblin, 1984; Bunce et al., 1990).

Rawal et al. (1982) reported a decrease in lens total protein levels in senile cataract. But the mechanism of decrease in lens total proteins is not completely understood. Rawal et al. (1982) also found a decrease in total soluble protein in senile cataract. This implies that a portion of soluble proteins is converted to insoluble ones.
Bhat et al. (1991) observed a significant decrease in insoluble proteins in brown lenses as compared to yellow lenses though they did not find any alterations in the total proteins. Based on this result they concluded that insolubilisation of lens soluble proteins takes place in senile cataractous cases along with the pigmentation. Truscott and Augusteyn (1977a), and Bando and Obazawa (1990) observed a remarkable insolubilisation of proteins in the lens with cataracta brunescence regardless of their low or high glutathione content. Vann Hard et al. (1980), and Bando and Obazawa (1990) were of the opinion that the conversion of soluble to insoluble fraction is progressive as the colour of the lens nucleus intensifies. This is especially apparent in brunescent type lenses where nearly 70% of the protein is insoluble, whereas in normal lenses of comparable age only 11% of the protein is insoluble. Garner and Spector (1978), Bhat (1982) reported an increase in insolubilisation of lens proteins without any change in the total lens protein.

The cataractogenesis is marked by the appearance of a high molecular weight (HMW) protein which is an intermediate between soluble and insoluble proteins (Jedziniak et al., 1973; Spector et al., 1974; Jedziniak et al., 1975). Pirie (1968), Anderson and Wright (1978) and Augusteyn (1981) were of the opinion that large amounts of insoluble proteins are derived either from
soluble proteins or structural proteins. Hightower and Reddy (1982a, 1982b) proposed that Ca\textsuperscript{2+} induce the formation of aggregates of high molecular weight proteins. It can be argued that the accumulation of HMW and water insoluble proteins cause light scattering which is an immediate cause of cataract. But Spector (1984) reported that it is not only the formation of large amount of HMW protein and water insoluble protein which is sufficient to cause opacification but a change in the quality of proteins may also alter the refractive index.

The aggregation and insolubility of proteins are due to the formation of covalent and noncovalent disulfide bonds or disulfide bond formation with glutathione or due to lysine modification, dityrosine crosslinks and lower molecular weight (LMW) peptide formations, which in turn unite with high molecular weight proteins through disulfide bonds (Truscott and Augusteyn, 1977a, 1977b; Augusteyn, 1979; Harding and Crabbe, 1984; Chylack, 1984; Spector, 1984; Kamei, 1990; Bando and Obazawa, 1990; and Bunce et al., 1990).

Garner and Spector (1980) proposed that oxidation of membrane proteins occurs prior to cytoplasmic proteins. The membrane proteins bind with cytoplasmic high molecular weight disulfide protein aggregates through a 43,000 kilo dalton (KDa) extrinsic membrane protein in nuclear cataracts. As far as the cortical cataract is concerned
the linkage to the membrane does not occur (Spector 1983). The disulfide protein aggregates that are linked to the membrane by 43 KDa protein may be enormous with molecular weights of more than 5,000 KDa (Augusteyn, 1979). The proteins of this size are capable of scattering light. As the number of these proteins increases, they alter the quality of retinal image and thereby reduce the visual acuity (Chylack, 1984).

A decrease in water-soluble proteins, a substantial increase in water-insoluble proteins and a gradual disappearance of low molecular weight crystallin proteins do occur in the normal lenses during aging. The disappearance of low molecular weight crystalline proteins is accompanied by the production of more and more high molecular protein aggregates (Spector, 1984 and Hockwin, 1985). These aggregates do not contain disulfide bonds. Hockwin (1985) and Kamei (1990) were of the opinion that the high molecular weight protein aggregation in normal aging lens is achieved by the involvement of calcium ions and glucose present in the lens.

The concentration of serum total proteins decreases 1.3 fold in individuals with cataract as compared to controls. But the total proteins remained almost the same at each stage of maturation of cataract (Goswammy, Mathur and Agrawal, 1971).
As mentioned earlier the biochemical characteristics of cataract is reflected mainly due to the formation of high molecular weight insoluble protein aggregates in lens. This is because of the different oxidative processes experienced by the human system in day to day activities. Under normal physiological conditions, the "antioxidant enzyme defence system" protects the lens and erythrocytes from the oxidative process (Ohrloff, Hockwin, Olson and Dickman, 1984; Giblin et al., 1985; Hockwin, 1985; Rathbun and Bovis, 1986; Bando and Obazawa, 1990; and Bhat et al., 1991).

The enzymes GSH-PO, GSH-R and G6PD take part in the defence against the different forms of oxygen released during oxidative stress in ocular tissue (Giblin et al., 1985). Bhat (1993) reported that the stabilisation of the free radical is governed by the "antioxidant system". GSH-PO is one of the antioxidant enzymes which decomposes \( \text{H}_2\text{O}_2 \) into water and it also catalyses the oxidation of GSH to GSSG (Mills, 1957; Pirie, 1965; Reddy, 1971; Srivastava, Lal and Ansari, 1980; Fecondo and Augusteyn, 1983; and Bando and Obazawa, 1990).

GSSG thus formed is normally reduced back to GSH by GSH-R, using NADPH as a cofactor (Augusteyn, 1981; and Cheng, Chylack and Sang, 1983). NADPH is regenerated from \( \text{NADP}^+ \) in G6PD catalysed reaction where glucose 6-phosphate
is converted to 6-phosphoglucono-Δ lactone (Bhat et al., 1991). G6PD then couples with GSH peroxidase (Figure 3) (Mills and Randall, 1958; and Cohen and Hochstein, 1963). GSH-R maintains GSH, protein sulphydryl groups and GSH-PO in its reduced state (Srivastava and Beutler, 1973; Weimer and Neims, 1975; Augusteyn, 1979; Cheng and Chylack, 1980; Bhat et al., 1991).

GSH - PO

\[ 2 \text{GSH} + \text{H}_2\text{O}_2 \rightarrow \text{GSSG} + 2 \text{H}_2\text{O} \]


Figure 3 Glucose 6-phosphate dehydrogenase coupling with glutathione peroxidase

As the age advances, the chance of cataract formation increases with a substantial decrease in the activities of various enzymes. Therefore, the lens becomes more susceptible to toxic oxidant reactions (Fecondo and Augusteyn, 1983; Rao et al., 1983; Ohrloff et al., 1984; Rathbun and Bovis, 1986; and Zhang and Augusteyn, 1994).