CHAPTER 3 REVIEW OF LITERATURE

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3.1 Introduction

Cesium compounds and their behaviour have generated considerable interest principally due to the increasing exposure of living systems to radioactive Cs following increasing nuclear activity. The initial areas of investigation have been i) the general effects as compared with other alkali metals in metabolism, transport and enzyme activation; ii) the toxicity, uptake and retention of the radioactive forms of Cs in different organisms, as related to the uptake and passage through the food chain and iii) use of Cs compounds in treatment and therapy, particularly of mental disorders. Later the work was extended to the relative effects of the radioactive forms and the stable forms and application of the interaction between them in counteracting harmful effects.

The toxicology of Cs compounds has assumed importance due to the observation that Cs+, both in radioactive and non-radioactive forms, enter easily into the plant and animal systems and finally the food chain. Cs+ is then transferred to the human system and deposited in muscles and other soft tissues, giving a relatively long, though individually variable, half-life. The biochemistry of Cs+ is of fundamental importance in devising methods for reducing the body content of radioactive Cs+ (Sastry and Spalding, 1968).

In assessing the transport of Cs in food chains, the amount of stable Cs available requires to be taken into account. Stable Cs determines to a large measure the rate of transport of Cs in systems where the radionuclide is sufficiently aged to be in equilibrium with stable Cs. Since soil is known to contain some stable Cs (see section on distribution of this article), the uptake of radioactive Cs is usually affected from the soil. Small applications of stable Cs to the soil can greatly increase plant uptake of radioactive Cs, probably by carrier effect (Nishita et al., 1965). Simultaneous application of stable and radioactive Cs to the soil increased the uptake of Cs by bushbean, Phaseolus vulgaris, by an
order of magnitude (Wallace et al., 1982). Large applications of stable Cs, on the other hand, can also decrease uptake of $^{137}\text{Cs}$ by isotope dilution. $^{137}\text{Cs}$ appears to get fixed on or in the clay lattice with time, becoming less available (Nishita et al., 1965). These factors affect the cycling of Cs in the ecosystems.

The Chernobyl accident focussed attention on the possible radiation hazards of radioactive Cs through accidental causes. $^{134}\text{Cs}$ and $^{137}\text{Cs}$ were located in dust samples in Thessaloniki (Misaelides et al., 1987); in rainwater collected in Nijmegen (Beentjes et al., 1987); in grasslands at southwest England (Gilbey et al., 1987). High concentrations were measured in a number of species of fungi from Germany (Kuyper, 1987; Dietl and Breitig, 1988). Even after a year, the effective dose equivalents for $^{137}\text{Cs}+^{134}\text{Cs}$ ranged between 6 and 44 μSv for workers in French nuclear installations. This amount is similar to the evaluation based on environmental measurements made within the first few weeks of Chernobyl accident (Anonymous, 1987). Direct exposure to two women in Kiev resulted in a committed effective dose equivalent of 0.4 mSv, the biological half-life of Cs being 60 days (Beentjes et al., 1988). In Sweden, a marginal increase of the existing dose from natural causes was recorded in farmers up to a year after the accident (Stenke et al., 1987).

### 3.2 Distribution

#### 3.2.1 In nature

In soil, variable amounts of Cs have been reported from different parts of the world. In 22 samples of arable soils tested, the Cs content ranged from 0.3 to 25.7 mg/kg of dry soil (Bertrand and Bertrand, 1949). The metal was located mostly in podzol soils upon pegmatites, gneiss and biotite; sulphate soils and rendzinas upon andesite from Moravia. Only traces were found in certain black and brown soils (Pelisek, 1947). A sample of desert soil from Nevada, USA contained 4 μg per g soil (Wallace et al., 1983).

In an assessment of perturbations of the geochemical cycles of metals by Society, Cs is grouped with Li and Rb. The scale of perturbation is nil at global level, but enhanced at regional and local levels due to mobilisation of crustal metals like soil and dust. The most diagnostic environment is sediment in coastal areas. The metals are soluble and toxic in excess but significant exposure is regarded as not likely (Andreae et al., 1985).

Neutron activation analysis of leached alkaline fly ash showed the presence of Cs, with Pb and other elements in the highly leached portions of residue
sequences, suggesting an association with the resistant internal silicon-rich glass matrix of the ash particles (Warren and Dudas, 1989). In two samples of loamy soil from India, Cs was more frequent in silty clay loam than in silty loam (Khan et al., 1988). Interestingly, the abundance of Cs in sea water is very nearly the same as in the earth's continental crust (Ehmann, 1968).

Cs content, estimated by flame photometry, in 16 samples of surface water from four oceans was 0.37 microgram/litre. The average concentration between 500 to 1500 metre depth was about 14% higher than the surface average, suggesting that the metal may be transported downward by particulate matter (Folsom et al., 1964). However in the North Pacific, typically deep water contained 1.4% lower average concentration than the surface water (Folsom et al., 1974). Analysis of 163 samples of mineral and thermal waters by electrothermal atomic absorption spectrophotometry showed the concentration of Cs to range between 4.5 to 148 \( \mu \)g per litre\(^{-1}\) (Bermejo-Barrera et al., 1989). Information on the occurrence of Cs as a pollutant in air samples is meagre, only one survey having been made in USA using the X-ray fluorescence method (Dittrich and Cothern, 1975).

2.2 In living systems

The distribution of Cs in living systems can be related to different factors. These include availability of Cs in the environment, like soil and water, and the presence of other elements, particularly potassium. The presence of stable Cs in the soil, in specific doses, also influences the uptake of radioactive \( ^{137} \)Cs by plants (Wallace et al., 1982).

Among algae, a detailed analysis of 14 species of the family Sargassaceae in four locations in Japan showed considerable variability in the content of Cs. \textit{Sargassam thunbergii} accumulated a higher amount than the other species (Ishikawa et al., 1986).

Relatively detailed information is available on the occurrence of Cs in higher fungi (Seeger and Shaut, 1981). The content was determined in 433 species (1166 samples) of European wild fungi, including Ascomycetes and Basidiomycetes, by flameless atomic absorption spectroscopy. It ranged from less than 0.1 to 308 mg/kg dry weight with an average of 7 mg/kg. The highest concentrations (308 mg/kg dry weight) were recorded in \textit{Cortinarius alboviolaceus} (family Cortinariaceae) from Sweden, followed by Clavariaceae, Rhodophyllaceae and Strophariaceae. The amounts in Helvellaceae and Lycoperdaceae were low. However, marked fluctuations were also recorded
within the same species grown in the same location, indicating the modifying effects of other factors, probably climatic ones, on the uptake of this element. The higher content of Cs in the fungi was to some extent related to the soil content. In general, the amount of Cs was usually highest in the flesh of the cap in the fruit body and the lowest in the gills or more rarely in the stem. The distribution was related to the type of the tissue. An earlier study of Saccharomyces cerevisiae (yeast) by energy dispersion X-ray microanalysis of thin sections had shown that the intracellular distribution of Cs and the allied elements K and Rb was similar. Their total concentration in the cytoplasm (190 mg/kg fresh weight) was about equal to that in the nucleus and twice that in the vacuole (Roomans and Severs, 1976).

Neutron activation analysis was used to measure Cs in grass samples from mining districts (Becker et al., 1975) and rice species (Teherani, 1987) marketed in Austria. The values did not show any significant variation in the latter, ranging from 0.016 to 0.032 ppm.

The accumulation of Cs, as also other trace elements, has been estimated in several parasites and other hosts. In general, helminths, like Fasciola hepatica belonging to different taxonomic groups, use the elements differently, possibly related to the specific metabolism of both the host and the parasite and also the biogeochemical environment (Gabrashanska, 1987; Damyanova, 1988). Larvae of class Trematoda were seen to accumulate Cs so that the amount was correspondingly reduced in the invaded host freshwater snails, like Lymnaea stagnalis (Gabrashanska, 1989). Earlier some evidences had been obtained of interrelationship of the Cs content in the body wall of Ascaris suum with other elements, notably Na and K (Ince, 1976). A comparative study of the distribution of the alkali group metals in marine animals had shown that muscle cells selectively accumulated K, Rb and Cs from extracellular fluids. Distribution of Rb and Cs in these cells was related to a certain extent to the specialisation of muscle fibres for the performance of phasic activity (Nesterov and Skul'skii, 1965). In the North Pacific Albacore, concentration of Cs was 26.75-2.35 in liver and 37.10-0.72 in muscle respectively (Hansen et al., 1978). Detailed investigations on distribution of Rb and Cs in fresh water migrating marine fishes shows a relationship with the type of the tissue (Skul'skii et al., 1967). The value of Rb/Cs in the muscle tissue of fishes is almost the same as in the preceding link of the food chain (Kanevskii and Fleishman, 1971).
A direct relationship was noted between food intake and Cs concentration in yellow-fin tuna (Thunnus albacares) (Olson and Boggs, 1986). Significant positive correlation was observed between K and Cs concentration in all tissues studied excluding kidney (Ito et al., 1986). In laboratory bred rats, given 0.025 ppm Cs dry weight in diet, the amounts present in the different organs (as ppm dry weight) were trace in lung, 0.028 in brain, 0.036 in liver, 0.043 in spleen, 0.069 in heart and 0.062 in kidney (Sato and Kato, 1979). In an earlier experiment, where the diet contained 0.032 Cs ppm dry weight, Cs values for kidney and liver were higher but for the heart was lower (Maziere et al., 1977), indicating that the amount accumulated is associated closely with the amount in the diet. Cs content of blood (as μg/kg) was 0.42 in plasma and 1.82 in erythrocytes in another set of rats on diet similar to the first one. The amounts of Cs in kidney and liver were however much lower (Gawlik et al., 1989), indicating the role of factors other than dietary ones. Analysis of bovine tissues shows the highest concentration of Cs in the forepart of the animal body (buccal and shoulder muscles, tongue, oesophagus) (Decowski and Malwinska, 1967). In human systems, as in other higher animals, Cs is a biologically important trace element due to its relationship with K in different biochemical and physiological processes. The amounts detected in serum and packed blood cells were about 0.74 and 4.82 μg/kg net weight respectively (Versieck et al., 1977). The relative quantities in pure and impure platelets were 54.8 ± 19.2 and 35.2 ± 13.8 respectively (Kasperek et al., 1979). In an earlier study of Cs, in stable and radioactive forms, from human tissues of cadavers in England, stable Cs in the bone occurred in the same proportion as in soft tissues (9 to 20 μg/g wet weight). The estimated amount of body Cs located in calcified bone was between 2 to 7% (Harrison et al., 1963). In a study (Rundo, 1964), of autopsy material and in vivo, Cs was observed to be widely distributed throughout the human body, mainly in the soft tissues. Uptake from gastrointestinal tract was rapid and essentially complete. Excretion was mainly by the urine, but there was a continuing loss through the feces, irrespective of the mode of exposure. The whole body retention of the element can be expressed by a two-component exponential function of time. An average of 10% of a single oral dose is excreted within one to two days, but the major part has a half-life between 50 to 150 days. This variability may explain the wide range of Cs contents reported from fallouts. More recent studies give a median value of $3.7 \times 10^{-8}$ ppm for Cs in human bone, which is uniform for both sexes but varies significantly between
child and adult (Lin and Wen, 1988). A single report is available on the presence of Cs in trace amounts in human milk from Australian women (Cummings et al., 1983). The amount of Cs in human tissues has been related to age in several cases. It has been shown to increase with progressing age in nearly all organs, except the skin which had been suggested as related to storage (Persigehl et al., 1977). In brain, however, the proportion of Cs shows no consistent trend with age, unlike K, P and Rb (Markesbery et al., 1984).

The levels of Cs have, in certain cases, been associated with disease conditions. In brain tissues from schizophrenic cadavers, an increase in Cs has been reported (Corrigan et al., 1990). Significant difference (P ≤ 0.05) has been observed in concentrations of Cs from 40 bulk brain samples, from patients with Alzheimer's disease, as compared to controls (Ehmann et al., 1986). In Alzheimer's disease, persistent imbalances are seen for the univalent cations Na, K, Rb and Cs, supporting the hypothesis that the disease is due to membrane abnormality (Thompson et al., 1988). Patients with major depressive disorder had reduced blood levels of Cs which increased towards normal on recovery (Ali et al., 1985). Contrary to earlier findings, no difference in Cs concentration was recorded between samples from manic, depressed, recovered manic, recovered depressed patients and normal controls, in urine, serum and blood by neutron activation analysis (Kumar et al., 1989). An increase in Cs content of blood plasma (+73%) and erythrocytes (+51%) was found in persons with renal disorders during the first stages of the disease. This suggests an effect of renal insufficiency on the Cs load of these patients (Gawlik et al., 1989). In 10 patients treated with chronic dialysis, Cs amount in serum is high before dialysis but decreases afterwards. There is no change in RBC (Cornelis et al., 1979). Total opaque (mature) cataractous lenses from 51 patients with senile cataract showed amounts of Cs related to the age of the donor (Theodossiadis et al., 1982). In a group of 40-59 year old males from Leningrad with histories of ischemic heart disease, a correlation was found between the content of trace element, including Cs in serum and levels of cholesterol, triglycerides and α-lipoprotein cholesterol in the blood (Il'in et al., 1982). Only one report is available on variation in blood Cs content between cancer patients and control but the data is inconclusive (Zdankiewicz and Fasching, 1976).
The half period of retention of radioactive Cs\textsuperscript{137} in the human body has been variously given as between 80 to 130 days with an average urinary excretion of 0.6\% of the body burden (Taylor et al., 1963). In some pregnant women, the biological half-life was seen to be 30 days and in their infants after birth of only 25 days (Bengtsson et al., 1965).

1.3 Uptake and Accumulation

3.3.1 Soil-Plant-animal-human chain

The exposure of human systems to Cs is considerably influenced by its incorporation into the food chain, which, in part, is determined by the transfer from soil to plants (Boikat et al., 1985). The extent of transfer depends on a number of factors. Some are well worked out like the species of the plant, growing conditions, soil properties and agricultural methods (Bundesminister, 1980). Other factors are not so well known (Romney et al., 1981). Fixation in the lattice structure of clay minerals is the most important factor for the biochemical cycling of Cs in terrestrial ecosystems (Schulz, 1965; D'Souza et al., 1972). The degree of fixation influences the subsequent long term availability of Cs to plants and depends on the type and portion of clay minerals (Gebhardt et al., 1981). Agricultural methods also influence the root uptake of Cs (Gulyakin and Yudintseva, 1962; Mistry et al., 1973; Tahir and Stewart, 1975; Handl and Kuhn, 1980). Ploughing of the soil, for example, mixes the superficially deposited Cs into subsoil layers. The transfer of Cs is similar between different marshy soils but is almost twice or more on podzol, which contains low total K, low clay and fine silt (Boikat et al., 1987). The degree of transfer also decreases with the age of the Cs deposit in the soil (Cline, 1981). In permanent pastures, the pH and amounts of organic carbon, exchangeable K and total Ca, do not effect the Cs transfer significantly (Boikat et al., 1987). The entry into the food chain and finally into the human system may be directly through fodder into animals used for meat and milk.

3.3.2 Uptake in plants

In algae (Chlorella kessleri and Scenedesmus obliquus), value for accumulation of Cs was found to be 2.9 (Stary et al., 1983). In various hydrophytes, including plankton and benthic algae and some members of Potamogetonaceae, from the Lithunian freshwater basin, the process of absorption of various radionuclides including Cs\textsuperscript{137} by different cell components was studied with reference to the role of the plant in radionuclide migration (Marchyulenene, 1987).
In yeast cells, the translocation of Cs at low pH is by three sites across the cell membrane, of which the interaction of Cs is only with the double electrical layer (Derks and Borst, 1979). The amount of Cs uptake by mushroom is higher due to the large surface of the mycelium. The absorption of Cs by lichen, being probably by the mycobiont, is less than that of the fungi (Eckl et al., 1986). A more efficient retention of Cs$^{137}$ was recorded in lichens from Brunswick, Canada, probably due to physiological uptake as a proxy for K. An inverse relationship between Cs$^{137}$ and K$^{40}$ activities is seen in lichen (Ellis and Smith, 1987). The accumulation of alkali metals, including Cs, showed a high level of correlation with taxonomic characteristic of 62 plant species collected from 9 sites in temperate forests of Japan. A marked association of Cs (8.2 ppm) was detected in leaves of Lastrea japonica, which was 6 times higher than species with the lowest concentrations (Memom et al., 1983).

In bean plants, Cs enters the roots and reaches the protoplasts of the epidermal cells, the speed of penetration being increased in the presence of K (Levi, 1970). The concentration ratio for Cs in trifoliate leaves of bush beans (*Phaseolus vulgaris*) varied from 8.67 (in presence of high K) to 0.96 (low K). The Y values (effect of concentration versus uptake) for Cs in plant parts were consistently near one, indicating Cs uptake to be directly proportional to its concentration in the nutrient solution. Roots accumulated 6 times more Cs than did leaves (Wallace, 1983). The penetration of Cs through isolated *Prunus armeniaca* leaf cuticles takes place by diffusion and is impeded by charge interaction between the solute and charge sites in the penetration pathway (Macfarlane and Berry, 1974). The upward movement of Cs in the xylem and redistribution from the leaves of *Lycopersicon esculentum* (tomato plants) showed a delay with respect to the redistribution of newly imported Cs from the source leaf of about 16-20 hours. However, the presence of fruit clearly caused large differences in net Cs delivery into the leaves (Wolterbeek and Bruin, 1986; Macfarlane and Berry, 1974). The lateral escape of Cs from the xylem seems to be proportional to the surface area of the xylem vessels and is apparently controlled by its transport across the cell walls of the transport channels (Wolterbeek et al., 1985). Cs uptake in roots of winter wheat was found to follow a dual pattern similar to K in barley. The solution to root transfer factor decreases in relation to an increase in the substrate concentration of the metal. At substrate concentrations equivalent to carrier-
free Cs concentration, however, the solution-to-root transfer factor is linear (Shaw and Bell, 1989). The movement of Cs from the parent trees to the seedlings of *Liriodendron tulipifera* was followed from floral parts of inoculated trees, through seed maturation and into the components of germinated seedlings. Cs$^{137}$, in both fruit and seedlings (cotyledons) followed pathways paralleling those of sugars and other translocated organic substances which may be stored in the tissues, later used to sustain early seedling growth. This shows that Cs may be transferred from the parent trees to second generation plants (Witherspoon and Brown, 1965).

3.3 Uptake, retention and excretion in animals

Transport of Cs in animals is actively dependent on the intracellular concentration of K ions. The ability of single neurons of the snail, *Planobarlius corneus* to accumulate Rb and Cs varies in the presence of ouabain *in vitro*. In such cases, the passive uptake of these two metals is related to intracellular K concentration and the K diffusion potential plays a major role (Skul'skii et al., 1987). The short circuited midgut from the larvae of *Hyalophora clerapia* can actively transport Cs, together with Rb and K from blood to lumen. Cs and K compete in the transport mechanism. High Cs:K values facilitate active transport of Cs; a ratio of 1 facilitates K and of 0.1 prevents transport of Cs (Zerahn, 1970). The application of Cs (2000 ppm) to tobacco budworms, *Heliothis virescens* eggs, revealed that individual eggs contained detectable levels of Cs (68%) alone. The latter was reduced by 10% over a seven day period. Cs concentration could be detected in whole bodies, wings and head capsules of both treated males and females (Hayes, 1989). The uptake of Cs by beetle larvae (*Cryosoma knabi*) feeding on willows was estimated to be 7-16 mg dry weight of plant per larvae per day under field and 9-10 under laboratory measurements (Crossley, 1966). The accumulation of Cs in the muscle tissues of perch (*Perca fluviatilis*) was found to be slightly higher than for roach (*Rutilus rutilus*) (Kanevskii and Fleishman, 1971).

When embedded frog muscles are exposed to various concentrations of Cs, the deposition of Cs occurs in specific protein sites in the A-bands and Z-lines of myofibrils (Edelmann, 1981). It is suggested that Cs ions, like other alkali metals, are not free in cell but are absorbed on $\beta$-carboxyl side chains of cell proteins (Edelmann, 1986; 1983). Administration of 40 mM CsCl to rats for periods up to 15 days in drinking water led to rapid uptake of Cs into fibres in red soleus and in pale vastus lateralis muscles. When Cs-rich muscles were
immersed in plasma for 30 mins from the same animal containing ouabain and bubbled with N and membrane potentials were measured, the very striking accumulation of Cs in red muscles in contrast to pale ones probably was not due to shower efflux of Cs but to a much faster influx of cation (Kernan, 1969; 1972).

Following intravenous administration of CsCl to laboratory rats, the total excretion of Cs was cumulative, between 50 to 20% of the dosage in 4 days. Fecal excretion was relatively slow and urinary between 27% of the dosage in 4 days. The maximum excretion was in the first 24 hours. The fraction of the metal excreted into bile did not depend on the dose administered. The bile/plasma concentration ratio was close to 1, and for liver/plasma above 1, indicating that the metal concentrated in the liver. The tissue distribution after 2 hours of Cs is given in the table below (Gregus and Klaassen, 1986).

<table>
<thead>
<tr>
<th>Dosages (mg/kg)</th>
<th>3</th>
<th>10</th>
<th>30</th>
<th>100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>4.00</td>
<td>3.76</td>
<td>4.20</td>
<td>4.06</td>
</tr>
<tr>
<td>Kidney</td>
<td>7.43</td>
<td>7.28</td>
<td>6.13</td>
<td>5.90</td>
</tr>
<tr>
<td>Spleen</td>
<td>2.52</td>
<td>2.57</td>
<td>2.62</td>
<td>2.51</td>
</tr>
<tr>
<td>Heart</td>
<td>6.41</td>
<td>6.39</td>
<td>6.00</td>
<td>6.16</td>
</tr>
<tr>
<td>Lung</td>
<td>2.61</td>
<td>2.60</td>
<td>2.69</td>
<td>2.78</td>
</tr>
<tr>
<td>Pancreas</td>
<td>3.35</td>
<td>2.77</td>
<td>3.53</td>
<td>2.89</td>
</tr>
<tr>
<td>Intestine</td>
<td>5.08</td>
<td>5.10</td>
<td>5.40</td>
<td>5.26</td>
</tr>
<tr>
<td>Stomach</td>
<td>2.31</td>
<td>2.18</td>
<td>2.09</td>
<td>2.15</td>
</tr>
<tr>
<td>Testes</td>
<td>0.441</td>
<td>0.394</td>
<td>0.383</td>
<td>0.459</td>
</tr>
<tr>
<td>Muscle</td>
<td>0.536</td>
<td>0.573</td>
<td>0.607</td>
<td>0.656</td>
</tr>
<tr>
<td>Bone</td>
<td>1.08</td>
<td>1.06</td>
<td>1.02</td>
<td>0.802</td>
</tr>
<tr>
<td>Brain</td>
<td>0.130</td>
<td>0.127</td>
<td>0.122</td>
<td>0.146</td>
</tr>
<tr>
<td>Blood</td>
<td>0.158</td>
<td>0.164</td>
<td>0.162</td>
<td>0.186</td>
</tr>
<tr>
<td>Plasma</td>
<td>0.141</td>
<td>0.132</td>
<td>0.127</td>
<td>0.136</td>
</tr>
</tbody>
</table>

Administration of semichronic (repeated) and acute injections of CsCl to mice and subsequent study of brain tissue showed that the accumulation was considerably higher with repeated treatment. The concentration in the brain remained elevated up to 6 days after the termination of treatment. The course was biphasic with the highest levels obtained 48 hours after treatment.
Treatment with Rb gives similar results but Li reached a peak much earlier and decreased progressively. These differences might be related to the duration of action of these three elements (Messiha, 1976). Cs accumulation in brain slices had been earlier suggested to depend on energy metabolism, similar to the accumulation of K (Arimatsu, 1969). The absorption of Cs in the gastrointestinal tract was found to be 6.4 to 79% of the daily intake. When bentonite (a clay mineral belonging to the filicilicates) was added to the diet, the intestinal absorption of Cs was drastically reduced (Van Don Hoek, 1976).

Specific activities of Cs$^{137}$ and Cs$^{133}$ were found to be similar in brain and muscle of the reindeer, Rangifer tarandus, though the concentration is higher in the latter tissue (Burovina, 1967).

In dairy cows, fed with Cs-contaminated hay for 5 weeks, the concentration in milk followed the Cs-intake rather quickly during the first week. After 5 weeks, the specific activity of Cs in the milk reached a level of 10.9nLi and levelled equilibrium. In general, 60% of the Cs uptake was excreted with the feces, 20% with urine and 5.0 to 8.8% with the milk (Steinwender, 1988).

In different mammals, including rats, the absorption of Cs$^{137}$ from the gastrointestinal system is rapid and its movement is affected by the presence of food (Moore, 1963). Excretion increases with reduction of environmental temperature, probably due to increased metabolic rate (Furchner and Richmond, 1963). Enhanced K intake above requirement reduced the half-retention time for Cs$^{134}$ at a decreasing rate (Johnson et al., 1968). Age influenced retention of Cs$^{137}$, but not uniformly (Miller et al., 1968). Chronic exposure of more than 400 days gave the highest levels in muscle and the lowest in fat. Concentration in the whole bone is related to the quantity and the state of the bone marrow (Furchner et al., 1964). It appeared rapidly in the fetus after oral administration to pregnant mice (Moore and Comar, 1963). Supplementation of diet with high levels of KCl and NaCl increased the rate of excretion of Cs$^{137}$, possibly due to diuretic action (Wasserman et al., 1963). Intraperitoneal administration of Cs$^{134}$ as chloride to mice induced the maximum Cs level in the kidneys, heart, lungs and liver in the first hour, in the muscle after 8 hours and in brain and blood after 24 hours. Transport is not wholly dependent on the ATPase system (Krulik et al., 1980).

Due to the health hazard from radio-isotope of Cs, interest was initially focussed on mainly whole body retention of radionuclides and their elimination (see review by Leggett) (Gawlik et al., 1989). The main pathway of excretion
was considered to be through the kidney, the ratio of urinary to fecal absorption being 10:1. Orally administered Cs\(^{137}\) is rapidly and almost completely absorbed; and is taken up by red cells from the plasma. The distribution in tissues decreases with time and the biological halflife was found, from analysis of excreta, to be between 50 to 60 days. The rate of excretion could not be enhanced by diuretics, corticosteroids or ion-exchange resins (Rosoff, 1963).

Both diet and environment are responsible for the accumulation of Cs in the human body. In 10 families from Japan the estimated daily intake of Cs in diet was 0.01 mg (Yamagata, 1962). The metal can also be deposited in the lung from inhaled particulate matter (Vanoeteren, 1986). Scalp hair was found to contain traces of Cs (Lai et al., 1987). In samples from Italy, Cs contents in human milk could be related to concentration in diet and drinking water (Clemente, 1982). Various factors have been offered to explain or predict the wide variation in the retention of Cs among humans.

The models for the retention of Cs in humans internal organs were derived from the rat model by modifying the rate constants of it to fit human data (Fujita, 1972). The retention pattern of Cs in adult humans may vary widely with age, sex, state of health, and may also show substantial variations for healthy persons of the same age and sex.

McCraw, (1965) developed a model that expresses the biological halflife of Cs as an increasing function of age throughout life. Total body K appears to be a reliable index to estimate retention of Cs. Cs follows the movement of K in the body and competes with K for transport across cell membranes, but substantial differences in the distribution and retention of Cs develop because of differences in transport rate across membranes (Leggett, 1986).

Cs\(^+\) is known to activate Na/K dependent ATPases in the absence of K\(^+\) (Skou, 1960; Whittam and Ager, 1964; Bader and Sen, 1966; Baker et al., 1969). It is transported into cells through pathways sensitive to ouabain inhibition. The amount of Cs\(^+\) needed to activate Na/K-ATPase and the transport rate varies, depending on the system studied. Usually Cs\(^+\) is less effective than the other alkali metal Rb\(^+\) in substituting for K\(^+\). In specimens with excitable membranes, Cs\(^+\) blocks the voltage-dependent channels that normally conduct Na\(^+\) or K\(^+\) ions. The resting permeability of Cs\(^+\) is however 0.3 to 0.1 times the K\(^+\) permeability (Mullins, 1975).
3.4 Effects of Cs on plants and lower organisms

3.4.1 Lower organisms

The growth of spiroplasma is inhibited by CsCl, the effect being inversely proportional to the concentration. At 150mM, growth of *Spiroplasma floricola* was inhibited totally, while limited growth was observed for *S. melliferum* (Chang, 1986). The bottom component of *B*$_{1a}$ of turnip yellow virus with a buoyant density of 1.45-1.43 g/ml, is converted to a more dense particle *B*$_{2a}$ following CsCl density gradient centrifugation. This conversion is enhanced by incubating the virus in CsCl solution at elevated temperature, which may be due to the exchange of polyvalent cations like Mg$^{2+}$ and spermine by Cs ions (Nookt *et al.*, 1982). When propagated in Cs-rich medium, poliovirus incorporated enough Cs atoms to shift its buoyant density from 1.34 to an upper limit corresponding to about 4200 Cs atoms/virion. The Cs-loaded virions were normal with respect to specific infectivity, neutralizability by specific antisera and electrophoretic profile of coat protein. If the RNA of the virus is exposed to Cs ions while the virus is being assembled, the poliovirus binds approximately the same number of Cs ions as human rhinovirus (Mapoles *et al.*, 1979). Cs ions bind to cell wall of psychrophylic microorganism (*Flavobacterium*) at different temperatures (Lembo, 1980). Cs was seen to be a non-competitive activator of the enzyme tyrosine-phenol-lyase present in *Citrobacter intermedius*. It affects the absorption and LD spectra of the enzyme and its complex with the quasi-substrate-alanine. The activation of tyrosine-phenol-lyase by Cs was connected with the increase of the active protonated form of the holoenzyme (λ max 420 nm) induced by Cs activators (Myagkikh, 1985) due to conformational rearrangements of the protein molecules (Demidkina and Myagkikh, 1989). Even in *Bacillus cereus*, the enzyme adenosine deaminase (EC 3.5.4.4) which is quite unstable, is stabilized by Cs, indicating that Cs influences the reactivity of some SH groups of the enzyme (Sgarrela, 1983). Ribosomal proteins of *E. coli* are dissociated under the influence of high CsCl concentrations from the ribosomes, turning normal 50S and 30S ribosomal subunits (37% protein) into protein deficient 43S and 28S particles called A particles (30% protein). Centrifugation of these A particles in CsCl leads to the formation of ribonucleoprotein particles even deficient in protein (20% protein). However, the dissociation of proteins from ribosomal particles under the action of high CsCl concentration appears to be reversible (Lerman, 1966). Another report suggests a competition between streptomycin and Cs
uptake by *E. coli* B cells. Cs ions however, were more weakly bound than streptomycin (Tamas et al., 1974). *E. coli* cells which contain a functional Kup (TrKD) system took up Cs\(^+\) with a moderate rate and affinity. Kup (TrKD) is a separate K\(^+\) uptake system with relatively little discrimination in the transport of the cation Cs. Regardless of the presence or absence of Kup, K\(^+\)-replete cells took up Cs primarily by a very low affinity mode, proportional to the ratio of the Cs and K concentrations in the medium (Bossemeyer et al., 1989). Cs (0.01 M) is observed to increase the rate of hydrolysis of ortho-nitropheno-β-D-galactosidase in *E. coli*, though higher concentrations are inhibitory. Cs induces inductive changes on the active site through binding with the substrate (Neville and Ling, 1967). Acyl-coenzyme A carboxylase from *Streptomyces erythraecus* was activated by Cs (Hunaiti and Kolattukudy, 1982). *Holococcus morrhuae* and *Halobacterium vallismortis* assimilate succinate in the formation of dicarboxylic acids and the rate of assimilation is hindered by CsCl (Tarasov et al., 1986). Growth yield of halotolerant bacterium A505 was inhibited by Cs and Li, unlike the other alkali metals; including Rb (Nagata, 1988). When bacteria are irradiated in solution of Cs salts, the lethal action was significantly higher than that obtained by irradiating the bacteria alone. Bacterial denatured DNA increases in buoyant density by about 0.045 density units in alkaline CsCl solution. Loss of water from the hydrated Cs-DNA complex occurs. One-third of the water is liberated by the DNA per degree elevation in temperature (Vinograd et al., 1963; 1965).

Growth of the algae *Chara fragilis* and *C. vulgaris* was increased in the presence of small amounts of Cs and Rb (Strauss, 1980). Outer membrane of the cells of *C. corollina* contain channels which are highly selective for K\(^+\). However, Cs is seen to reduce K currents in *Chara* at high \(C_D K^+ (Ca^{2+})\) channels. It mainly inhibited K\(^+\) inward current, in a strong voltage-dependent manner. The effective valence of the blocking reaction was often greater than one, increasing with higher external Cs and lower K\(^+\) concentrations. Selectivity of the channel to Cs varied, depending on the method of measurement, suggesting that ion movement through K selective channel may not be independent (Tester, 1988a,b,c). Cs is observed to activate glutamate dehydrogenase of *Chlorella pyrenoidosa* (Shatilov, 1976). Cs ions affected growth and induced clock-like banding in wild strains of *Podospora anserina* at low concentrations (0.04 mol/l) (Lysek, 1981).
In yeast, Cs stimulates the depression of phosphate transport produced by glucose to a lower extent than K (Pena and Ramírez, 1986). Toxicity of organotins towards the marine yeast *Debaryomyces hansenii* has been observed to be reduced by CsCl (Lawrence et al., 1989). Cs also inhibited the enzyme $\Delta^{24}$ sterol methyl-transferase present in mitochondria of yeast (Bailey, 1974). Cs is considered to be the most toxic among the alkali chlorides and inhibits growth of *Aspergillus niger* and *A. oryzae* (Kurita and Funabashi, 1983). It reduced the levels of the enzymes-acetamidase, histidase, nitrate reductase and urate oxidase in *A. nidulans* (Hynes, 1974) and inhibited ribonuclease present in *Ustilago sphaerogena* (Holloman, 1971). On the other hand, mutants of *Micrococcus varians* ssp. *halophilus* were able to grow in CsCl when isolated from a complex medium (Kamekura and Onishi, 1982).

### 3.4.2 Higher plants

The toxic effect of Cs studied on tomato plants was seen to depend on two parameters: reaction affinity of the element to the organic fraction of the cell and the accumulation coefficient but low toxicity (Kabanov and Myanedov, 1974). However, hypocotyls of tomato seedlings, germinated both in light and dark, with CsCl, appeared as though they had been attacked by a virulent pathogen or wilt disease (Wolterbeek et al., 1985). CsCl when given at concentrations of 0.1 to 100 mm reduced the amounts of amino acid and ammonium nitrogen in tomato leaves related to the senescence (Kabanov and Myanedov, 1974). The metal accumulated in leaf, stem, root and apical point of tomato, suggesting the presence of constant absorption sites for Cs in these tissues (Myasoedov and Katanov, 1974). Though the germination frequency of tomato seedlings was high with CsCl solutions, yet root growth was inhibited. In addition, the hypocotyl hook region became adversely sensitive to white or red light. Hypocotyls of seedlings germinated in Cs solution in different light environment showed discoloration, pronounced twisting and severe suppression of extension (Kordan, 1985; 1987a,b). The mean dry matter content and drying rates of alfalfa (*Medicago sativa*) were increased by 0.2 M of Cs solutions (Panicera et al., 1989; Johnson, 1983). Cs was also observed to prolong the period of the leaf movement in *Oxalis regnellii*, depending on the ion concentration (Rinnan and Johnsson, 1986). Different concentrations of Cs were observed in the leaves of *Sapindus mukorosis*, *Aistonia scholaris* and *Diospyros embryopteris* as a consequence of airborne emission (Iqbal et al., 1990). The uptake of Na in the presence of Cs was enhanced at lower concentration and
inhibited at higher concentration in pea, cucumber and wheat plants. Stimulation was strong in wheat, less pronounced in cucumber and weak in pea plants (Shah, 1969). Zn absorption in wheat was depressed by Cs (Chaudhury, 1972). Germination frequency and germination energy of cucumber seeds were enhanced when grown in Cs. Activities of catalase and peroxidase were also enhanced, but not phenoloxidase (Vlasyuk, 1970). Wheat germ acetyl CoA carboxylase (Nelson and Stumpf, 1976, peroxidase and isocitric dehydrogenase and Halin'ska, Vlasyuk, 1971) were all activated by Cs. Cs affected the protein metabolism of sprouting seeds of wheat, intensifying the conversion of stored protein and the accumulation of structural and catalytic proteins (Vlasyuk et al., 1970). Chlorophyll synthesis was hampered, followed by shoot damage, when etiolated barley seedlings received Cs nutrition exposed to radiant energy (Marscher and Gunther, 1966). Cs nutrition resulted in inhibition of chlorophyll development and accumulation of protochlorophyllide in a following dark period. These changes in the chlorophyll development caused by Cs are closely related to changes in the fine structure of the plastids in the plants. The arrangement of the thylakoids in the typical grana structure can be scarcely detected in the plastids, and most thylakoids are swollen. These structural changes are associated with strongly depressed chlorophyll synthesis. Changes in the structural protein of the plastids, resulting from Cs nutrition, are primarily responsible for the decreased chlorophyll synthesis. The total pigment disintegrated and the barley sprouts died. Such harmful effects of Cs are mediated through photoinduced absorption of Cs ions, which change the conformation of protein molecules and disturb their normal functioning or, convert porphyrins to protochlorophyllide (Marscher, 1964; 1965, Rotfarb et al., 1970). The intensity of Cs has also been observed to increase the intensity of two fluorescence bands of pigment system I at 735 nm in spinach chloroplasts (Murata, 1971).

3.5. Effects of Cs on animal systems

3.5.1 Invertebrates

The activity of Cs is related to the concentration to which the system has been exposed. Recessive mutants of Paramecium tetraurelia have been shown to be sensitive to CsCl, in higher doses, together with RbCl and KCl (Cronkite, 1982). In the septal membranes of the median and giant axons of earthworm, which contain gap junctions, two types of channels were seen. One type, apparently a K+ channel, was blocked by Cs+ and had a unitary
conductance of 30-40 ps. The other, with a unitary conductance of 90 to 110 ps, could conduct Cs\(^+\) even in the presence of other divalent cations (Brink and Fan, 1984). In single neurons of the snail, *Helix pomatia*, the A-current K\(^+\) channels are permeable to Cs\(^+\) (Taylor, 1987). When external K\(^+\) ions are replaced by Cs\(^+\) the outward currents are reduced (Junge, 1982). A similar high permeability was seen for single glutamate-gated channels in locust skeletal muscle (Kits, 1988). The blockade of snail neuron K\(^+\) channels by other alkali metals, including Cs\(^+\), was found to depend on the voltage when studied using a voltage clamp and internal perfused techniques (Magura, 1986). Internal Cs, relative to internal K, alters Na current time course in *Myxicola* giant axons (Goldman, 1986). Application of Cs\(^+\) to the basal face of sensory epithelium of Lorenzinian ampullae of the Black sea skate, *Raja clavata*, suppressed spike response adaptation (Broun et al., 1985). Similar to K\(^+\), Cs\(^+\) can also produce a reversible abolition of the action current in the nerve of *Maia squinado*, but 3.2 Cs ions are needed to give the effect of one K ion (Cowan, 1934). Large concentration of Cs ions could block a small, but statistically significant, fraction of outward K current for potentials \(< 50\text{mV}\) positive to reversal potential in axons of the squid, *Loligo pealei* (Clay et al., 1983). The isolated gill cuticle of the shore crab *Carcinus maenas* showed a level of permeability to Cs\(^+\), higher than Rb, but lower than K\(^+\) (Lignon, 1987). A single report is available of the induction of metamorphosis of *Phronis psammosiphila* larvae (Phoronia, Tentaculata) by CsCl (0.06 M) (Herrmann, 1979). Pink Dollworm, *Pectinophora gossypiella*, raised on artificial diet containing Cs or on cotton plants sprayed with different doses of CsCl, showed the presence of Cs in the adults. Higher doses \((5 \times 10^{-2})\) of CsCl were however lethal (Moss and Wyk, 1982).

### 3.5.2 Lower vertebrates

External Cs blocks the adenosine 5'-triphosphate-dependent K channels in sarcolemma vesicles from frog skeletal muscle in a voltage-dependent fashion, the degree of blockage increasing with hyperpolarization. The Cs block is flicker, mean unitary current being reduced and open-level noise increased (Quayle et al., 1988). Similar results were obtained from frog sinus venosus trabeculae (Champigny and Lanfant, 1986). In frog skeletal muscle cells, Cs competed for the absorption sites normally occupied by K\(^+\) (Ling, 1977) and strongly reduced K conductance in frog atrial trabeculae (Taupignon et al., 1982). External Cs ions reduced K efflux in muscles incubated in Na containing medium, apparently by inhibiting the K:K exchange mechanism (Beauge, 1973).
Cs ions are possibly transported inwardly by an active process after first accumulating in a superficial reservoir (Beauge and Sjodin, 1968). Gradual increase of miniature end plate potentials was observed in frog neuromuscular junction. However, the potential decreased when low concentration of 6-40m of CsCl was applied (Ginsberg, 1968; Takikawa, 1989). Cs has been observed to increase the osmotic fragility of erythrocytes in dehydrated frogs (*Rana temporaria*) by affecting the water balance of the animal (Ermakova, 1970). Cs depressed pacemaker actively, conductivity contractility and vagal stimulation of frog hearts by replacing K (Jentgens, 1937). In frog skin, Cs blocked K transport by binding to site within the channel (Dewolf and Van Dricosche, 1989). Analysis of the Na⁺ kinetics shows that K⁺ and Cs⁺ participate in a Na⁺ exchange mechanism in direct proportion to their penetration across the cell membrane (Portella, 1966). *Bufo arenarum* eggs reared in Cs solution showed maximum anomalies at the blastula stage (Bustuoaba and Pisano, 1979).

Cs polarizes the skin of the fish *Kryptopterus*, producing a specific skin potential, but a dependence characteristic of its own. Both the skin potential and the potential of the sensitivity maximum lie near 0mV and are nearly equal (Roth, 1983). Summated neural responses were observed from the peripheral nerves of the lateral line organs in the goby, *Gobius giorinus*, in the presence of a threshold of \(-10^{-3}\) M Cs solution (Kawamura and Yamashita, 1983). Most of the intracellular K of turtle, *Testudo hermani* can be replaced by Cs. The intracellular accumulation of Cs possibly occurs via an active inward transport system which operates with the simultaneous efflux of Na (Guerin and Wallon, 1975). Isotonic Cs solutions depressed outward current of acetylcholine activated channels of chick myotubes. Dilution of internal Cs, 10-fold from 320-40mM, increased the permeability of the channel (Dwyer and Farley, 1984).

Since Cs is an industrially important element and exhibits properties similar to the other alkali metals, a large amount of information is available on the toxic effects of Cs compounds, using mammalian test systems. The reports are variable.

### 3.5.3 Mammals
Interperitoneal injection and oral administration in both rats and mice gave moderate toxicity, except the hydroxide (Cochran *et al.*, 1950; Johnson *et al.*, 1975). Even the hydroxide and iodide were less toxic than the corresponding salts of Rb and K. In most reports Rb compounds were found to
be more potent than Cs compounds in bioactivity and toxicity. However in one case greater chronic toxicity was reported for CsCl in rats than the other two elements (Eichelman et al., 1977). Higher amounts of CsCl and RbCl reduced the voluntary intake of alcohol by rats (Messiha, 1978). Toxicity of chloride, sulphate, carbonate and nitrate of Cs was observed to be low for all laboratory animals following all modes of administration. Of these the first two salts were even less toxic than the two latter ones (Bruk, 1964). When Cs was given intragastrically, subcutaneously and intraperitoneally to mice and rats, no signs of distress or of poisoning could be seen. In fact, some rise in the resistance of the animals to the repeated administration of Cs was observed. Subcutaneous injection of 26 mgm CaCl₂ resulted in excretion of 17.5-20% of the Cs in the first 24 hours, and 3% in the next 24 hours. 84-85% of the Cs is excreted in the urine and the remaining in the feces (Bruk, 1968; Walbum, 1929). Bruk (1969) later carried out elaborate experiments on the effects of Cs salts on frog, mice, guinea pigs, pigeons, rabbits and cats. All the salts were found to be toxic. Following intravenous injection, the toxicity of all the salts was twice that after oral route and 1.5 times that after subcutaneous route. Direct harmful effects of Cs compounds on mammals observed include acute and chronic poisoning and irritation of skin and mucous membrane. Cs₃AsO₄ was seen to be embryotoxic. Permissible levels in the air were suggested to be 0.03 mg/m³ for Cs₃AsO₄ and 0.3 mg/m³ for CsOH (Tarasenko and Lemeshevskaya, 1978).

Contrary to such toxicological and physiological behaviour, Cs has been clinically evaluated as an antidepressant of motor activity in mice (Yamauchi, et al., 1972). It reduces the isolation induced aggression (Eichelman, 1977) and decreases the analgesic action of morphine (Bulaev and Ostrovskaya, 1979). Multiple intraperitoneal injections of subcutaneous doses of CsCl to rats and mice daily for 4 to 56 days showed no significant difference from controls in tissues from lung, brain, liver, kidney and spleen of mice. In ileal tissue only, prominent lymphoid follicles were seen. A single high acute dose induced effects, more or less similar to the chronic one. Cs accumulates rapidly in both rat liver and kidney, and the amount of NaDH in rat liver was inhibited when CsCl was added to submitochondrial particles (Nalecz, 1978), and the 60S ribosomal subunits of rat liver were inactivated at a relatively low concentration (0.3 μm, Arpin et al., 1972). The levels of lipoperoxidation and glutathione were altered in livers of mice and rats, following application
of 40 mol/kg of Cs; related to dose and time of exposure (Caisova and Eybl, 1987). From a study of different animal circulatory systems, in vivo and in vitro, CsCl and Cs$_2$SO$_4$ were observed to cause negative chrono-, ino and dromotrophic reactions and at high doses, disturbance of rhythm and stoppage. The mechanism of Cs action is composed of direct and reflex effects on the vasomotor nerves, central and peripheral cholinergic components, adrenergic component and direct effect on the vascular system musculature (Bruck, 1969).

Cs has no known vital function. However, since the concentrations of Rb and Cs appear to show a similar level in rats, depending on the organ and the postnatal age, and Rb is known to possess unique neurophysiological characteristics in animal systems (Fieve et al., 1971), it was suggested that these two elements are essential to life (Sato, 1983). Cs ions activate chloride channels in cultured rat spinal cord neurons, possibly by acting directly on the extracellular surface of the neurons. The channels activated are the same type as are activated by GABA and the inhibitory neurotransmitter glycine through an as yet unidentified receptor (Hughes et al., 1987; Smith and McBurney, 1989). The locus coeruleus neurons of rat showed anomalous rectification strongly dependent on the external K$^+$ concentration, which could be blocked by external Cs$^+$ (Osmanovic and Shefner, 1987). External Cs ions also had a depressive effect on the acetylcholine (Ach) induced inward current in rat adrenal chromaffin cells in culture (Hirano et al., 1987). Cs$^+$ is shown to disturb the normal neuromuscular transmission of stimulus (Sica et al., 1967) in rats. In cats immobilised by myorelaxants intracellular injection of Cs$^+$ ions in pyramidal neurons of sensorimotor inward current (Kakoya et al., 1988). Similar blockade of various K conductances by internal Cs$^+$ ions was also recorded in cat motoneurons (Pul and Werman, 1981).

Regional changes occurred in brain glutamic acid and $\alpha$-amino-butyric acid when rats were injected with CsCl (Gottsfeld, 1976). Effect on creatine kinase, 5' nucleotidase, phosphodiesterase deaminase was very low, and inhibition of AMP protein kinase was seen in brain (Krulik et al., 1978; 1980; 1981). Acute action leads to autonomic upset in mice and multiphasic excitant-depressant effects on the central nervous system (Pinski et al., 1981) Some workers had earlier described excitant effects for Cs ion in the CNS of mammals (Johnson, 1972; Jenner et al., 1975; Messiha, 1978a,b; Rastogi et al., 1980). Spontaneous motor activity in mice was
accelerated by chronic administration of Cs (Yamauchi et al., 1972). Bose and Pinsky (1980, 81, 83ab) revealed a depressant component to CNS responses and a possible antipsychotic-like activity. Cs is also seen to interfere with acquisition of pole-climbing conditioned avoidance response and showed a mutual synergism of CAR suppression with chlorpromazine and haloperidol (Bose and Pinsky, 1983b).

Irradiation with Cs^{137} induced additional DNA-synthesis in the neocortex tissue and the neurons of the cerebral cortex of rats. In 14 day old rats, the induced synthesis stopped two hours after irradiation whereas in the cortex of 60 day old rats and in neurons of rats of both age groups, it proceeded for 3 to 3.5 hours (Ivanov et al., 1987).

In rat erythrocytes, the affinity of Cs to the binding sites is decreased by Cs (Gyorgyi, 1974). Taylor (1971) observed the extrusion of Na produced by Cs in the rat myometrium. In isolated rat osteoclasts, Cs could suppress the inward currents activated by hyperpolarizing voltage commands (Sims and Dixon, 1989).

Differences were reported in the retention of Cs^{137} and Cs^{144} in male and female rats following intraperitoneal injections, related to the age of the animal, but not to a significant level. The retention in the skeleton was most affected (Kulikova, 1966).

A combination of Cs salts (carbonate or chloride), zinc gluconate and vitamin A showed repression of tumour growth in colon carcinoma implanted in BDF_1 mice (Tufte and Tufte, 1984).

In cats, Cs salts at doses from 5 mg/kg to the lethal dose (160 mg/kg) caused a bi-phasic action with an initial brief hypotension followed by moderate hypertension, bradycardia and weakening of the cardiac contractions (Bruk, 1969). Diastolic depolarization is caused by a Cs-sensitive component (Rubenstein and Lipsius, 1989). The most striking effects of internal Cs on cats were a marked prolongation of the falling phase of action potentials, a large reduction in the amplitude after hyperpolarization, and a considerable increase in the size of the delayed depolarization. Similar effects were observed in dogs (Hanich et al., 1988; Brachmann et al., 1983). Internal Cs apparently blocks voltage-dependent K conductance of spike repolarization (Puil and Werman, 1982). Cs induced early and delayed afterdepolarization,
ventricular arrhythmia and atrioventricular block in feline, canine and sheep Purkinje fibres (Graham et al., 1989; Isenberg, 1976).

Cs is adsorbed on cell membranes in guinea pig hearts (Edelmann, 1971) and protects against myocardial ischemia in guinea pigs by facilitating restoration of developing pressure and reducing the "reperfusion contracture" (Shul'zhenko et al., 1989). It releases superoxide from guinea pig peritoneal neutrophils (Matsumota et al., 1986). The addition of Cs to brain cortex of guinea pigs led to considerable increase in the respiration of the brain mitochondria optimally at 10-50mM (Sugawara and SatoBuka, 1965). Cs ions allowed Purkinje cell dendrites to depolarize to a range of 20-30mV, and to reverse both climbing and parallel fibre responses (Kimura et al., 1985). Cs increases excitability in the left atria but in lower concentrations (2 M), it decreases excitability in the papillary muscles (Prasad and Mirdha, 1973). However, the cochlear function of guinea pigs showed toxic effects related to Cs ion concentration (Lotz et al., 1976). On the other hand, guinea pig spermatozoa are unable to fuse with eggs unless exposed to a millimolar concentration of extracellular Cs (Yanagimachi and Bhattacharya, 1988).

Cs salts stimulated immunobiological properties and promoted mobilisation of adaptive, protective and compensatory reactions in rabbits (Tagdishi and Aliev, 1973). In rabbit sarcoplastic reticulum vesicles, Cs reacted with the cation transport system only from the outside (Yamamoto and Kasoli, 1982). ATP diphosphohydrolase from the sarcoplasmic reticulum increased bimolecular lipid membrane (oxidized cholestrol) conductance several hundred-fold in the presence of Cs (Shamoo and MacIannan, 1974). Enolases were also activated in rabbit by Cs (Kornblatt and Klugerman, 1989). Rates of Ca transport and Ca$^{2+}$ dependent ATP hydrolysis of the reticulum of rabbit and dog cardiac membrane were stimulated by Cs (Shigekawa and Pearl, 1976). The magnitude of Na pump current in sheep is an S shaped saturating function of Cs. Hill coefficient of the current was 1.73 for Cs and the pumps were activated by external Cs (Glitsch et al., 1989).

Survival rate of cultures from monkey heart cells was increased by the action of CsCl and taurine given together in equimolar concentration (Akhalaya et al., 1976). Cs replaces intracellular K in the bovine heart mitochondria (De Gomez et al., 1976).
3.6 Effects of cesium on human system

In general, Cs ions block K channel in biological membranes in a voltage-dependent manner. For example, external Cs blocks inward current with little or no effect on outward current (Clay and Schlesinger, 1984).

Experiments using in vivo NMR studies have shown that in biological samples: i) intra and extracellular Cs⁺ ions have different chemical shifts that are readily resolved; ii) spin-lattice relaxation times for intracellular Cs⁺ ions are significantly shorter than values of extracellular ions; iii) in red blood cells Cs⁺ ions are taken up at approximately one third that of K⁺ ions; iv) this rate is decreased in the presence of the cardiac glycoside ouabain (Davis et al., 1988).

One of the earliest works on human is by Girard and Peyre (1934), who claimed that injection of Cs eosinate salt would protect against anaphylactic shock when given intravenously.

The mechanism for volume regulation in hypotonic media was analysed in human peripheral mononuclear (PBM) cells. Generally hypotonic swelling was followed by regulatory volume decrease. In high K⁺ hypotonic media, shrinkage was absent and a second swelling phase was observed. With Cs⁺, shrinkage was observed at lower dilutions and secondary swelling at higher ones (Cheung et al., 1982). Alpha-amylase activity of dialyzed and non-dialyzed human granulocytes was activated by 0.02 M of Cs (Zakrzewska, 1982). The volume of human red cells contracted on administration of Cs (Hall and Ellory, 1986).

The effects of Cs on the rate of ouabain binding and on the Na-K pump were examined in human red blood cells. In Na-containing solutions, Cs decreased the rate of ouabain binding. The kinetics of these effects were similar to those for the activation of the pump. In Na free (choline substituted) solutions, the rate of ouabain binding was increased by Cs (Hobbs and Dunham, 1978). Correspondence analysis of data segments of both lungs of eight individuals about the concentrations of 22 trace elements showed that Cs is one of the elements, the concentrations of which are highest in the lungs of the oldest individuals. It was assumed that the element was enriched in the tissue by inhaled dust, accumulated and deposited in an insoluble form (Vanoeteren and Cornelis, 1986). The ability of the cations Cs⁺ and Rb⁺ to substitute for K⁺ as agents for causing contraction was studied in segments of human uterine muscle. The tension produced by Cs⁺ was identical to that produced by K⁺ (Rosenblum et al., 1966). In human granulocytes, CsCl increased the activity of alpha-amylase to the same level as chlorides of
Na, K and NH$_4$ (Zakrzewska, 1982). Unlike Li and Rb, however, the stabilising effect of Cs on the cell membrane of human erythrocytes, following electric field-mediated hemolysis, is rather insignificant (Mangal and Vijh, 1987). During studies on Cs blockade in a calcium-activated potassium channel from smooth muscle, internal blockade was found to be voltage-dependent and can be explained on the basis of a Cs$^+$ binding to a site that senses 54% of the applied voltage. External Cs$^+$ however blocks the channel in micromolecular amounts and the voltage dependence of the blockade is a function of Cs$^+$ concentration. The channel itself behaves as a multi-ion pore. External Cs$^+$ blockade can be relieved by increasing the internal K$^+$ concentration, but can be enhanced by increasing the external K$^+$. A model is suggested incorporating a "knock on" of Cs$^+$ by K$^+$ (Cecchi et al., 1987). Functional changes in the cardiovascular and nervous systems were reported in workmen employed in the production of Cs and Rb (Khosid, 1967).

Cs levels were reduced in blood from depressive patients which increased toward normal on recovery (Ali et al., 1985). The response to Cs is altered in disease conditions, as for example, in streptozotocin-induced diabetic mice (Fujii and Nomoto, 1987). In a group of twenty nine patients with brain neoplasms, leukaemia and other non-cerebral malignancies and thirty two non-malignant control patients, some with neurological and others with non-neurological conditions, the mean Cs value in the control group was 3.8 g/l. There was no difference in the value between the groups investigated (El-Yazigi et al., 1988). This result is of interest in view of the fact that Cs, though not directly involved in the causation of cancer, yet is reported to be an activator of one or more enzymes (Gooddy et al., 1974). It has been measured in brain tumour tissue (Mitchell et al., 1984) and in the cerebrospinal fluid of patients with motor neurone disease (Mitchell et al., 1986) or amyotrophic lateral sclerosis (Schicha et al., 1972). In patients with Alzheimer's disease, persistent imbalance of univalent cations like Na, K, Rb and Cs has been reported in the brain, particularly in amygdala, hippocampus and nmb. This observation suggests a membrane abnormality related to the disease (Thompson et al., 1988; Ehmann, 1986).

Cs did not alter brain superoxide dismutase (SOD) both in vivo and in vitro. In this behaviour it resembled K, but not Li (Shukla, 1987). Cs also differs in other behavioural patterns from alkali group metals. For example, in binding with membrane phospholipids, the binding forces decrease in the order Cs$^+$ $\rightarrow$ Rb$^+$.
→ K⁺ → Na⁺ (Cserhati and Szogyi, 1983). The binding selectivity of heparin for cations increases with an increase in the radius of the hydrated cation form, namely, Li⁺ → Na⁺ → K⁺ → Cs⁺ (Dais et al., 1989).

Cs has been used as a substitute for radium in the treatment of carcinoma of the cervix. In overall patterns, the results of the two are very similar (Jackson et al., 1989). The only report on the analysis of chromosomal aberrations in human lymphocytes after in vitro exposure to Cs¹³⁷ gamma radiation showed that the dicentrics, total acentrics and excess acentrics follow a Poisson distribution. The frequency is related to the dosage administered to a certain extent (Doggett and McKenzie, 1983). Animal models have been extensively employed in studying effects of Cs. However, in some cases caution is needed in interpreting the results to the human systems. For example, the transient nature of the arrhythmogenic action of CsCl injection in dogs make a systematic study of the acquired long QT syndrome observed in man difficult (Naybpour et al., 1989).

3.7. Other effects

No report is available on the effects of Cs salts on cell division or chromosomes.

3.8. Uses

The earliest report of the uses of Cs came from Walbum (1929) who claimed that 90% of the infectious diseases in mice can be cured by administering Cs. Cesium tetra-iodophenolphthalein was used by Johnson and Hitzort (1935) for gall bladder visualisation. The bandings of the G bands are produced by CsCl (Meisner et al., 1974). Cs is used in the preparation of membrane fractions from human cerebral cortex (Thompson et al., 1967) and as a storage material (Zolg et al., 1988). Porphyrin from barley seedlings is isolated in the presence of Cs ions (Rotfarb et al., 1970). Circulating red cell volume can be measured by Cs (Price et al., 1976).

One of the major applications of Cs is in the density-gradient centrifugation. This method has been utilised in the fractionation of coxsackie viruses (Schmidt et al., 1963), isolation of encephalomyocarditis virus (Goodheart, 1964); purification and concentration of small round viruses from human feces (Ashley and Caul, 1982); purification of bacterial DNA (Flossdorf, 1983) and plasmid DNA (Garger et al., 1984); isolation of mitochondrial DNA of macrospecies (Babykin and Zinchenko, 1984) and DNA of Sinapis alba (Capesius and Reiter, 1982); purification of mitochondrial DNA of Eukaryotes (Cornelius et al., 1988) and bacteriophage (Mirande et al., 1988; isolation of fungi, oocytes and sporozites (Karwowski, 1986; Kilani and Sekla, 1987) and RNA and DNA of Trichinella spiralis larvae (Zarlenga and Gamble, 1987); determining the distribution of DNA in the family Iridaceae (Beride and Antonov, 1984), and satellite DNA (Villalba and Ramirez, 1982); isolation and purification of yeast, bacteria, algae, higher plants and mammalian insect (Weeks et al., 1986). It is also extensively used as a pharmacologic agent (Bose and Pinsky, 1984). Cs in recent years has been used to protect plants from insects and fungus (Castro et al., 1990).