

CHAPTER - 6

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6. SUMMARY

Cadmium is a toxic metal. Human exposure to this metal is a result of its presence in soil, food, water, cigarette smoke, pollution due to burning of coal, erosion of rubber tyres, and the use of Cd as an anticorrosive coating for steel products. Experimental evidence obtained from controlled laboratory conditions suggests that Cd may function or may be an etiological factor for various pathological processes including testicular tumor, renal dysfunction, growth inhibition, chronic diseases of old age, atherosclerosis, cancer and hypertension. Though Cd causes a wide range of pathological effects, its role in hypertension has attracted much attention in recent years.

The impact of Cd on the environment is undoubtedly increasing (Lancet, 1976) and because hypertension is a common disease associated with high morbidity and mortality, it is important that the relationship, if it exists, be clearly delineated. Therefore, an investigation on the effect of Cd on experimental animals is of considerable interest for the evaluation of its impact on the health of the general population and especially its contribution to the health problem.

Thus, the present work on 'Some pharmacological investigations of cadmium' is aimed at studying various actions of this metal on rat blood pressure and on isolated tissues.

6.1. IN VIVO STUDIES :

6.1.1. ACUTE EXPERIMENTS :

Acute intravenous administration of CdCl_2 (0.5 and 1 mg/kg) in female rats produced a short-lived fall in blood pressure followed by an increase in blood pressure which persisted for several minutes.

Acute intraperitoneal administration of CdCl_2 (0.5 and 1 mg/kg) produced a pressor effect which persisted for 30 minutes.

The acute pressor response to CdCl_2 (i.v. and i.p.) was not blocked by phentolamine, hexamethonium, propranolol, atropine, reserpine or indomethacin.

The pressor response to CdCl_2 (i.v. and i.p.) was significantly blocked by calcium channel blockers such as verapamil (0.5, 1, 2 mg/kg) or nifedipine (0.25 and 5 mg/kg).

The blood pressure response to low doses of NA was significantly reduced after the intravenous administration of CdCl_2 . However, the blood pressure responses to ANG II, isoprenaline and ACh were not modified by either intravenous or intraperitoneal administration of CdCl_2 .

6.1.2. CHRONIC EXPERIMENTS :

Chronic administration of CdCl_2 (0.5 and 1 mg/kg/day, i.p.) for two weeks produced significant elevation of blood pressure in female rats. This was accompanied by significant reduction in body weight of the animals.

Bilateral adrenalectomy in rats did not prevent hypertension induced by the chronic administration of CdCl_2 . Chemical sympathectomy produced in rats by the chronic administration of guanethidine did not prevent CdCl_2 -induced hypertension.

Chronic oral administration of captopril also did not prevent the hypertension produced by the chronic CdCl_2 administration.

However, chronic verapamil or nifedipine treatments significantly prevented the CdCl_2 -induced hypertension.

Adrenalectomy, chemical sympathectomy and chronic captopril treatment did not prevent the acute pressor response to CdCl_2 in rats.

However, in rats pretreated chronically with verapamil or nifedipine, the acute pressor response (i.p. or i.v.) to CdCl_2 was prevented.

6.2. IN VITRO STUDIES :

6.2.1. ACUTE EXPERIMENTS :

6.2.1.1. RAT HIND QUARTER PREPARATION :

Intra-arterially administered CdCl_2 produced elevation of perfusion pressure in rat hind quarter preparations.

The increase in perfusion pressure produced by acute intra-arterial administration of CdCl_2 was not blocked by phentolamine or reserpinization. However, verapamil reduced the increase in the perfusion pressure produced by intra-arterial CdCl_2 administration.

6.2.1.2. RAT ISOLATED AORTA :

$4.8 \times 10^{-8}\text{M}$ and $4.8 \times 10^{-7}\text{M}$ CdCl_2 potentiated the response to KCl with a significant increase in pD_2 value in rat isolated aorta. Similarly, $4.8 \times 10^{-8}\text{M}$ CdCl_2 also significantly potentiated the response to NA with an increase in the pD_2 value. Higher concentrations of $1.44 \times 10^{-5}\text{M}$ CdCl_2 produced significant rightward shift of the dose-response curve of KCl and NA with the depression of maxima in rat aorta.

$4.8 \times 10^{-8}\text{M}$, $4.8 \times 10^{-7}\text{M}$ and $1.44 \times 10^{-6}\text{M}$ CdCl_2 produced small contractile response in rat isolated aorta. However, this response was blocked by the removal of Ca from the bathing medium. A higher concentration of CdCl_2

($4.8 \times 10^{-6}M$) did not produce any such contractile effect. The dose response curve was bell-shaped.

6.2.1.3. RAT ISOLATED PORTAL VEIN :

In rat isolated portal vein $CdCl_2$ $4.8 \times 10^{-7}M$ potentiated the response to KCl without modifying that to NA. However, $4.8 \times 10^{-5}M$ $CdCl_2$ shifted the dose-response curves of NA and KCl to the right with the suppression of the maximal responses.

6.2.1.4. RAT ISOLATED VAS DEFERENS :

In isolated rat vas deferens, $1.44 \times 10^{-8}M$ $CdCl_2$ potentiated the KCl response without modifying that to NA. However, higher concentrations of $CdCl_2$ reduced the responses to KCl and NA.

6.2.1.5. RAT ISOLATED ANOCOCCYGEUS MUSCLE :

In isolated rat anococcygeus muscle, $4.8 \times 10^{-6}M$ - $4.8 \times 10^{-5}M$ of $CdCl_2$ shifted the dose-response curves of KCl and NA to the right. This inhibitory effect was enhanced when the Ca concentration in the perfusion medium was reduced to 25%.

6.2.2. CHRONIC EXPERIMENTS :

Rats chronically treated with $CdCl_2$ showed an increase in the basal perfusion pressure in hind)quarter preparation.

In preparations from rats chronically treated with CdCl_2 there was also significant potentiation of the perfusion pressure to NA. Similarly the sensitivity to NA was also increased in isolated aorta of CdCl_2 -treated rats.

6.3. CONCLUSION :

The present study suggests that Cd in low doses might increase the availability of Ca ion for the contractile process. In addition Cd might mimic Ca ion and produce a direct contractile effect on vascular smooth muscle. These mechanisms might contribute to the acute pressor and chronic hypertensive effect of Cd observed in the present study and also reported by others.

It is therefore, concluded that Cd might produce its effect either by a direct action on vascular smooth muscles and/or by altering the fluxes of Ca ion.

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