

# INFLUENCE OF NATRUM MURIATICUM ON ADRENOCORTICAL (ZONA GLOMERULOSA) STEROIDOGENESIS\*

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## INTRODUCTION

Sodium is an important electrolyte essential for all animal kingdom to regulate the normal body function. Natrum muriaticum (Nm) is a homoeopathic drug which is prepared from common salt and is widely used in homoeopathic treatment with a remarkable efficacy for various types of sufferings. A large number of symptoms of Nm have been reported by providing on healthy human beings and it is observed that among all the symptoms, the desire for salt of the patient was more or less constant. From this point of view it is logical to assume that Nm patient may have some gross disturbances in the salt regulation of body. However, the exact mechanism for the regulation of salt balance in the body is far away from clear. But, on this topic an extensive research work is continuously going on and time to time different theories regarding salt regulating mechanism of the body were put forward.

In 1953 a sodium retaining steroid—Aldosterone—was discovered and from that time till date an exhaustive research work is continuing to explore the regulatory mechanism of aldosterone. However, now it is established that aldosterone takes an immense role in the regulation of salt balance of the body and it is synthesised in the cells of the zona glomerulosa. It has been observed that a low-sodium diet increases aldosterone production in normal human being<sup>1</sup> and this finding was soon confirmed by others<sup>2,3</sup>. Extensive studies on the mechanism involved in the increase in aldosterone biosynthesis during changes in the state of total body sodium have been made in several species. It is now established that sodium depletion increases aldosterone secretion in man<sup>4,5,6</sup>, sheep<sup>7,8,9</sup>, dogs<sup>10,11</sup>, and rats<sup>12,13,14,15</sup>. The mechanism whereby sodium depletion increases aldosterone secretion have been the subject of discussion and even debate. However, the consideration of the above facts in collaboration with desire for salt in case of Nm patient lead to suggest that there may have been some imbalance in salt regulating mechanism of the body. A large number of Nm symptoms have been reported<sup>16</sup> on the basis of drug proving on healthy human beings in different homoeopathic potencies. But, a little attention was paid to evaluate the physiological phenomena through which the Nm in homoeopathic potencies acts in the body economy. Therefore, the present experiment has been undertaken to find

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out whether Nm in homoeopathic potencies possess any role in the alteration of adrenocortical (zona glomerulosa) steroidogenesis or not.

It has been reported earlier that  $\Delta^5$ - $3\beta$ -hydroxysteroid dehydrogenase ( $\Delta^5$ - $3\beta$ -HSD) is a key steroidogenic enzyme<sup>17</sup> of the steroid producing gland and its activity varies proportionately according to the rate of synthesis of steroid hormones. Glucose 6-phosphate dehydrogenase (enzyme of pentose phosphate pathway) is absolutely essential in the steroid producing gland as it is the major supplier of NADPH<sup>18</sup> which is required for steroid hydroxylation. The present experiment was primarily based on histochemical demonstration of  $\Delta^5$ - $3\beta$ -HSD and glucose 6-phosphate dehydrogenase (G6-PDH) in adrenal cortex of albino rats.

#### MATERIALS AND METHODS

Twenty mature female rats (whister strain) weighing 150-170 g. body weight were used and they were equally divided into two groups. Animals were kept under standard laboratory conditions (temp. 30°C; 12 hr. illumination/day) giving free access to food and water. One group of animals was fed Nm 30 potency (0.01 ml) daily for 4 days and the other group of animals was fed with 96% alcohol in the same amount and in the same manner and treated as controls. Four days after the application of the last dose all the animals were sacrificed by decapitation. Fresh cryostat sections of adrenal (20  $\mu$ m) were used for the demonstration of  $\Delta^5$ - $3\beta$ -HSD activity using dehydroepiandrosterone as substrate<sup>19</sup> and G 6-PDH<sup>20</sup>. Parallel sections were incubated at identical conditions (at 37°C for 30 min.) in substrate free media to check the specificity of the reaction. All the sections were fixed and mounted in glycerol jelly for microscopic observations.

#### RESULTS

Figs. 1 and 3 showed histochemical localisation of  $\Delta^5$ - $3\beta$ -HSD and G 6-PDH in the adrenal cortex of control rats respectively. Enzyme activities were noted in all the three zones of the adrenal cortex. After treatment with Nm intensity of staining reaction for  $\Delta^5$ - $3\beta$ -HSD and G 6-PDH were increased in zona glomerulosa of adrenal cortex. (Figs. 2 & 4).

#### DISCUSSION

Fig. 5 showed the schematic diagram of aldosterone biosynthetic pathway and the site of action of different enzymes involved in it. It can be seen in the Fig. 5 that  $\Delta^5$ - $3\beta$ -HSD acts in the conversion of  $\Delta^5$  pregnenolone to progesterone. Fig. 1 showed the histochemical activity of  $\Delta^5$ - $3\beta$ -HSD in the adrenal cortex of control rats. Following administration of Nm  $\Delta^5$ - $3\beta$ -HSD activity in the zona glomerulosa of the adrenal cortex remarkably increased in comparison to control rats (Fig. 2, compare with Fig. 1). It is established that  $\Delta^5$ - $3\beta$ -HSD activity directly varied in relation to steroid hormone production. Therefore, increased activity of  $\Delta^5$ - $3\beta$ -HSD after treat-



Fig. 1 Histochemical demonstration of  $\Delta^5$ -3 $\beta$ -HSD in the adrenal cortex of control rats.  $\times 100$ .

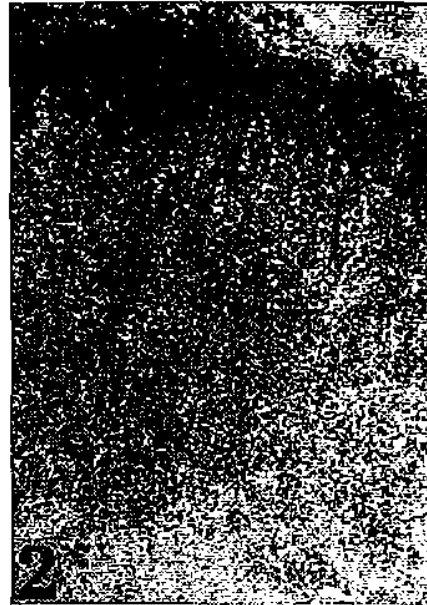


Fig. 2 Remarkable increase of  $\Delta^5$ -3 $\beta$ -HSD in the zona glomerulosa of adrenal cortex after treatment with Nm, compare with Fig. 1.  $\times 100$ .



Fig. 3 Histochemical demonstration of C6-PDH in the adrenal cortex of control rats.  $\times 100$ .

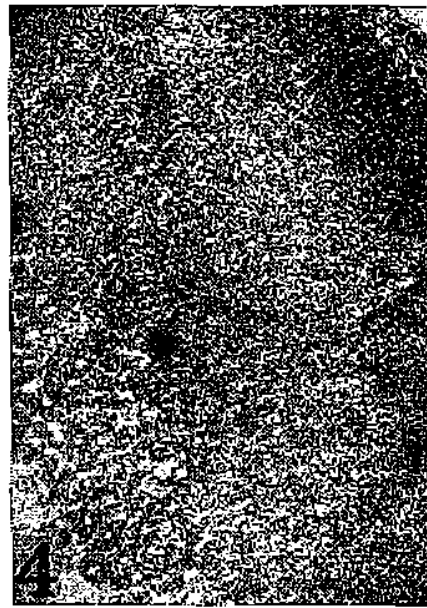
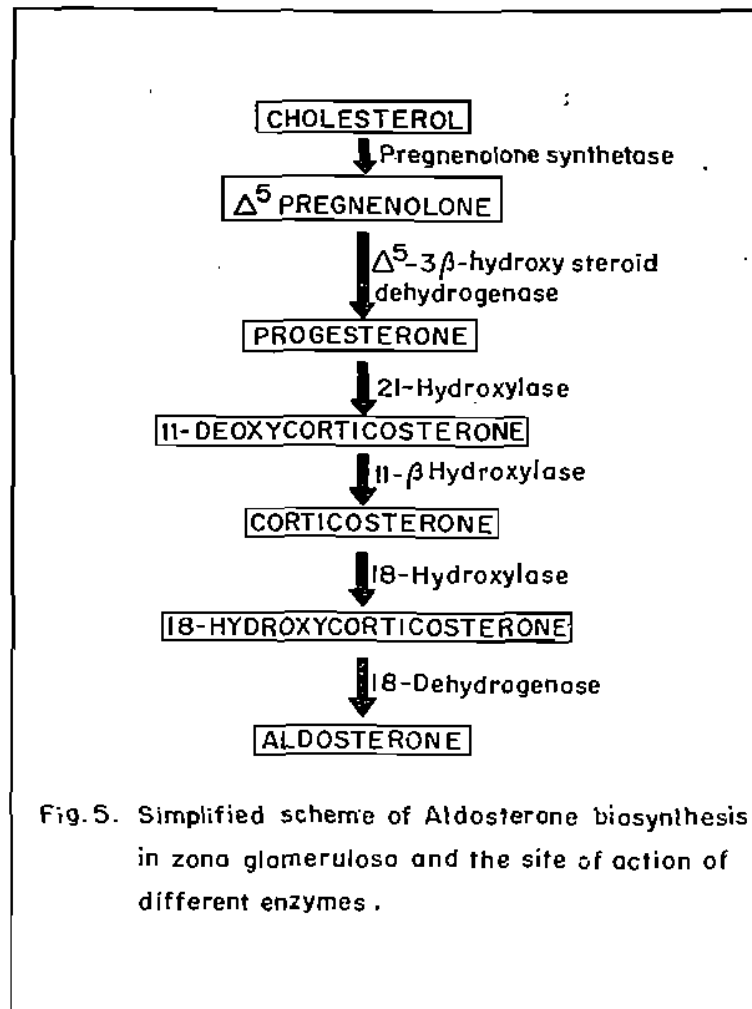


Fig. 4 Increased activity of C6-PDH in the zona glomerulosa after treatment with Nm, compare with Fig. 3.  $\times 100$ .



ment with Nm suggested an increase in the steroid hormone production in the zona glomerulosa.

The presence of highly active pentose phosphate pathway (carbohydrate metabolising pathway) in the steroid producing gland have been discussed elsewhere. G 6-PDH is an important enzyme of the pentose phosphate pathway which generates reduced nicotinamide adenine dinucleotide phosphate (NADPH) which is essential for steroid hydroxylation. Histochemical preparation showed an increased activity of G 6-PDH in the zona glomerulosa of adrenal cortex after treatment with Nm (Fig. 4, compare with Fig. 3). A number of previous workers have reported earlier that increased steroidogenesis accompanied with accelerated activity of G 6-PDH. Therefore, on con-

sideration of the above facts in collaboration with the present findings, it is suggested that treatment with Nm in 30th potency resulted in an increased synthesis of steroid hormone in zona glomerulosa (aldosterone).

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**Editorial comment:** The author's studies of the action of Natrum mur. in 30th potency on the zona glomerulosa of rats and establishment of a direct physiological relationship between it and the levels of aldosterone are very interesting. However, his reference (16) to the symptoms recorded in drug provings of Natrum mur. in homoeopathic potencies on human beings is not a record of merely the physiological action of the drug on human tissues, but a study of its dynamic action on his entire economy including the changes observed in the more nebulous mental plane. The profession

would have been interested to know from Dr. Paul, if he had extended his field of observation to assess how many of the symptoms observed in provings were attributable to the physiological action of *Natrum mur.* and how many fell outside the scope of such observation. Such reporting should form a convention of every research paper sent for publication in a homoeopathic journal to set clearly the limitations posed by the scientific inquiry in the present state of knowledge to ascertain the pathogenetic action of the homoeopathic drugs which it regards to be dynamic, lest the scientific world gets away with the idea that the two are synonymous!

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