EFFECT OF GUGGULIPID ON NOREPINEPHRINE BIOSYNTHESIS OF MONKEY TISSUES

MADHULIKA SRIVASTAVA, SWARN NITYANAND and NARINDER K. KAPOOR
Central Drug Research Institute, Lucknow 226 001, India.

ABSTRACT

The effect of chronic feeding of guggulipid, a hypocholesterolemic agent of plant origin, on the levels of catecholamine and dopamine β-hydroxylase (DBH) activity of brain and heart tissues of rhesus monkeys has been studied. The levels of norepinephrine, dopamine and activity of norepinephrine biosynthetic enzyme DBH were found to increase progressively with increasing dose of guggulipid. The data suggest that increase in catecholamine biosynthesis by guggulipid is one of the possible mechanisms to explain lipid lowering activity of this plant product.

INTRODUCTION

GUGGULIPID the gum resin exudate from *Commiphora mukul*, is claimed to be efficacious in the treatment of rheumatoid artheritis, obesity and allied disorders[1]. Hypocholesterolemic effect of *Commiphora mukul* resin and its fractions has been reported from our laboratory[2-6]. Earlier, garlic oil, another lipid lowering agent, was observed to enhance the catecholamine biosynthesis of rabbit tissues (Unpublished data). Berkowitz *et al*[7] have reported an increase in norepinephrine (NE) concentration in all tissues and of NE and serotonin (5-HT) in the brain by an antiatherosclerotic agent, pyridinol carbamate. In our previous reports, propranolol induced changes in catecholamine biosynthesis of different parts of rat brain[8] and heart[9], have been investigated. Since catecholamines are known to play an important role in atherosclerosis[10-12] and coronary heart diseases, it was considered of interest to investigate the effect of lipid lowering agent, guggulipid, of plant origin on the regulation of norepinephrine (NE) biosynthesis. The present paper reveals the action of guggulipid on the levels of NE and dopamine-β-hydroxylase (DBH) activity of monkey brain and heart.

MATERIALS AND METHODS

Rhesus monkeys were taken from Central Drug Research Institute animal colony and maintained on normal standard diet adequate in protein, vitamins and minerals. They were divided in 4 groups and treated with guggulipid (prepared in mucilage and water) orally for 6 months as follows:

Group I—4 monkeys were given normal diet served as control.

Group II—4 monkeys were fed with guggulipid, 60 mg/kg body weight.

Group III—4 monkeys fed with guggulipid, 120 mg/kg body weight.

Group IV—4 monkeys were given guggulipid, 240 mg/kg body weight.

Catecholamine estimation: The levels of DA and NE were estimated according to the alumina adsorption method of Malherbe[13] details of which are described in our earlier reports[8,14].

DBH assay: The enzyme activity was assayed spectrophotometrically by the method of Nagatsu and Udenfriend[15] using tyramine as substrate and its details description is given earlier[8,16].

RESULTS

As shown in table 1 the catecholamine levels and DBH activity of brain were increased regularly. Feeding of a low dose (60 mg/kg body weight) caused an increase of 32% in DA level while NE level was increased only by 18%, however, DBH activity was stimulated by 58%. On increasing the dose to its double quantity there was observed approximately 85% increase of both NE and DA level with 2.8 fold increase in DBH activity as compared to control group. On further increasing the dose, no marked enhancement was observed in NE level and its biosynthetic enzyme activity, however, DA level increased by 1.9 and 3.5 fold as compared with group III and group I respectively.

Alterations in catecholamine levels and DBH activity of monkey heart by feeding of guggulipid are also represented in table-1. An increase of 57.4 and 62.3% in levels of DA and NE respectively was observed by feeding of 60 mg guggulipid/kg body weight. DBH activity was stimulated by about 2.5 fold. On doubling the dose, DA and NE levels were further increased by 45.7 and 64.6% respectively with 1.8 fold rise in DBH

Table 1 *Catecholamine level and DBH activity in brain and heart of guggulipid fed monkeys.*

Group	Brain			Heart		
	Catecholamine level (μg g wet. tissue) (Mean ± S E.)		Unit activity of DBH* (Mean ± S E)	Catecholamine level (μg/g wet. tissue) (Mean ± S.E)		Unit activity of DBH* (Mean ± S E.)
	DA	NE		DA	NE	
I	0 98 ± 0.04	0.75 ± 0.03	1.48 ± 0 04	0.66 ± 0.02	0 83 ± 0.05	1.73 ± 0 08
II	1.29 ± 0 10	0 89 ± 0.05	2.34 ± 0 08	1 04 ± 0.08	1.34 ± 0.09	4 31 ± 0.15
III	1.82 ± 0.14	1.39 ± 0.09	4 10 ± 0.23	1.52 ± 0.11	2.21 ± 0 17	7.60 ± 0.23
IV	3 44 ± 0 19	1.45 ± 0.11	4 18 ± 0.21	2.11 ± 0.18	3 45 ± 0.18	8.95 ± 0.24

* 1 unit is expressed as 1 nmol octopamine formed per mg protein per min. P with respect to control < 0.01.

activity. These increases in NE, DA level and DBH activity were found to be 2.3, 2.7 and 4.4 fold respectively on comparison to control group. Again, in IV group the DA and NE level and DBH activity were observed to be increased further showing 38.4, 56.3 and 17.7% rise respectively. When compared with the normal group increase in DA, NE levels and DBH activity was 3.3, 4.2, and 5.2 fold respectively.

DISCUSSION

The data show that feeding of guggulipid to monkeys results in an almost progressive increase in the catecholamine levels and DBH activity of brain and heart. It is very likely that there is an increase in the levels of NE as a consequence of its enhanced synthesis via DBH enzyme. Our results are in close agreement with those reported by Berkowitz *et al*[7] for an antilipaemic agent pyridinol carbamate showing increase in NE level of rat heart, brain and mesentric artery. It was suggested that pyridinol carbamate may effect the cardiovascular system directly by modifying the NE content of heart and vascular tissue and possibly, indirectly, by raising the concentrations of brain NE and 5-HT. In our studies, the changes in catecholamine levels and DBH activity by lipid lowering agent may be due to its direct effect on cardiovascular and central nervous system.

Our studies showed that increase in NE biosynthesis of brain was noticeable upto feeding of 120 mg guggulipid/kg body weight showing maximum effect of the compound at this dose. However, DA level increased as usual on further increasing the dose possibly due to stimulation of tyrosine hydroxylase enzyme by guggulipid. Nevertheless, the implication of other enzymes like monoamine oxidase and catechol-o-methyltransferase, in regulation of catecholamine levels cannot be ruled out.

Earlier an increase in catecholamine biosynthesis of rabbit tissues was investigated using guggulipid and garlic oil, the lipid lowering agents of plant origin (unpublished data). Also we observed decrease in catecholamine levels and DBH activity of rabbit and monkey tissues by feeding them with high fat diets including cholesterol (unpublished data). It was assumed that decrease in catecholamine biosynthesis was due to deposition of fat leading to the alterations in metabolic activity of cells.

It can be concluded from our findings that changes in catecholamine levels and DBH activity induced by guggulipid appear to be related with its hypolipidaemic activity.

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