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TABLE 1. *IN VITRO* INHIBITION OF CREAM XANTHINE OXIDASE BY 4 (OR 5)-DIAZOIMIDAZOLE-5 (OR 4)-CARBOXAMIDE AND RELATED COMPOUNDS

Compound	Per cent inhibition* (average of values of 5 experiments)	
	1×10^{-6} (M)	1×10^{-5} (M)
Diazo-ICA[a]	70	100
Cysteaminyl-Diazo-ICA[b]	51	100
Cysteinyl-Diazo-ICA[c]	48	100
AICA·HCl[d]	—	0
AICA riboside[e]	—	0
Aza-AICA[f]	—	5
Thio-AICA riboside[g]	—	1
Formylthio-AICA[h]	—	9
Allopurinol[i]	39	94
2-Azahypoxanthine	—	17
6-Mercaptopurine	—	3
8-Azaguanine	—	3
Dimethyl-TICA·HCl[j]	8	21
Diazo-BS[k]	—	16
N-Ethylmaleimide	—	0

a, 4(or 5)-diazoimidazole-5(or 4)-carboxamide; b, 4(or 5)-(2-aminoethylthio azo)-imidazole-5(or 4)-carboxamide; c, S-(5(or 4)-carbamoyl-4(or 5)-imidazolyl azo) cysteine; d, 4(or 5)-aminoimidazole-5(or 4)-carboxamide hydrochloride; e, 1-β-D-ribofuranosyl-5-aminoimidazole-4-carboxamide; f, 4(or 5)-aminotriazole-5(or 4)-carboxamide; g, 1-β-D-ribofuranosyl-5-aminoimidazole-4-thiocarboxamide; h, 4(or 5)-formylaminoimidazole-5(or 4)-thiocarboxamide; i, 4-hydroxypyrazolo(3,4-d)pyrimidine; j, 4(or 5)-(dimethyltriazeno)imidazole-5(or 4)-carboxamide hydrochloride; k, diazobenzene sulfonamide benzenesulfonate.

* The inhibition measurements were carried out by the addition of graded amounts of the various compounds 0·4 ml to incubation vessel containing glycylglycine (0·1 M, pH 7·5) 2 ml, EDTA (1 μmole/ml) 0·4 ml, hypoxanthine (1·25 μmole/ml) 0·2 ml, the enzyme (20 unit) 0·5 ml and water 0·4 ml.

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Anti-convulsant action of anabolic steroids

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MUTUAL antagonism in rats between leptazol (pentylenetetrazol)-induced convulsions and the steroids, progesterone and desoxycorticosterone, has been reported.[1] It has also been shown that several steroids effectively antagonize electroshock seizures in rats by elevating the electroshock

threshold.[2-4] Recent evidence indicates that the anticonvulsant actions of progesterone, desoxycorticosterone and other steroids are not related to their individual hormonal activities.[5]

There is no clear evidence regarding the anticonvulsant action of anabolic steroids, although it has been shown[5] that norethandrolone, an anabolic steroid, is not an anticonvulsant even in high doses (300 mg/kg). Therefore the present study was undertaken to see whether or not the anabolic steroids act as anticonvulsants. There is no direct evidence that the anticonvulsant action of steroids may be correlated with the elevation of γ-aminobutyric acid (GABA) levels in brain. Thus it has been demonstrated that cortisol increases the susceptibility of rats to electroshock seizures without having any effect upon brain GABA levels.[6] The effect of anabolic steroids on brain GABA was also investigated in order to see whether their anticonvulsant effect may be related to elevation of brain GABA levels.

Male albino mice, weighing 20–30 g, were used in these experiments. The anabolic steroids investigated were methandienone (Dinabol, CIBA), 4-chlorotestosterone acetate and noradrosternolone phenyl propionate (Durabolin, Organon). The anabolic steroids (2 mg/kg) were injected intraperitoneally into mice. After 90 min, leptazol was injected intraperitoneally.

In studying the effects of these steroids on brain GABA levels, mice were sacrificed in the terminal stage of convulsions, brains were rapidly removed and frozen in dry ice. The control mice were handled similarly. Each brain was homogenized in 7·0 ml of cold 75% (v/v) ethanol and centrifuged. The clear supernatant was separated and the residue was reextracted with cold 75% ethanol and centrifuged. The combined supernatants were evaporated to dryness and the residue was extracted with a mixture of water–methanol–chloroform (0·5:1:1) and centrifuged. Free GABA in the extract was separated and determined by ascending unidimensional paper chromatography with water-saturated phenol as the solvent system.[7]

The results (Table 1) indicate that the anabolic steroids, methandienone, 4-chlorotestosterone acetate and norandrosternolone phenyl propionate, antagonized the leptazol-induced convulsions in mice. Of the anabolic steroids tested, methandienone showed the most powerful anticonvulsant action, followed by 4-chlorotestosterone acetate and then norandrosternolone.

TABLE 1. EFFECTS OF ANABOLIC STEROIDS ON LEPTAZOL-INDUCED CONVULSIONS IN MICE

Leptazol (mg/kg)	Pretreatment*	No. of mice used	No. of mice having convulsions	Convulsions (%)
40	Control	63	35	55·5
	Methandienone (2 mg/kg)	28	5	18
	4-Chlorotestosterone acetate (2 mg/kg)	26	26	23
60	Control	18	15	83
	Methandienone (2 mg/kg)	10	5	50
	4-Chlorotestosterone acetate (2 mg/kg)	10	6	60
	Norandosternolone phenyl propionate (2 mg/kg)	10	7	70

* Anabolic steroids, methandienone, 4-chlorotesterone acetate and norandrosternolone phenyl propionate, were administered intraperitoneally 90 min before leptazol administration.

Our experiments also show that these steroids, methandienone ($P < 0·1$), 4-chlorotestosterone acetate ($P < 0·05$) and norandrosternolone phenyl propionate ($P < 0·5$), had no significant effect upon brain GABA levels. This finding is supported by the observation that brain GABA levels probably are not well correlated with the action of most anticonvulsant or convulsant drugs. It has been demonstrated that the elevation of brain GABA levels does not necessarily imply a rise in the

threshold of convulsions.[8,9] It is also equally true that many substances are powerful anticonvulsants without having any appreciable effect upon brain GABA levels.[10]

On the basis of the above evidence, it may be assumed that the anticonvulsant action of anabolic steroids is probably due to other mechanisms controlling brain excitability, possibly involving electrolyte distribution.

C.S.I.R. Pharmacology Research Unit,
Department of Pharmacology,
Seth G.S. Medical College,
Parel, Bombay-12, India

S. G. KALYANPUR
S. R. NAIK
SAVITRI PAHUJANI
U. K. SHETH*

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* Reprint requests to Prof. U. K. Sheth.

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Etudes sur l'action biologique du benzo(a)pyrène — II
Effet de l'irradiation gamma sur l'induction d'hydroxylases microsomiales hépatiques par le benzo(a)pyrène

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L'ADMINISTRATION de benzo(a)pyrène (BaP) à des rats en croissance détermine, endéans 24 hr, un accroissement important des enzymes microsomiaux hépatiques qui hydroxylent cet hydrocarbure[1,2]. On a montré par des moyens divers et convergents la réalité d'une synthèse accrue de protéines dans le déroulement de ce phénomène, ainsi d'ailleurs que des modifications morphologiques du reticulum endoplasmique. Un certain nombre d'autres processus métaboliques doivent entrer en jeu pour expliquer l'ampleur des transformations biochimiques constatées ainsi que l'absence de spécificité des systèmes enzymatiques induits Il est vraisemblable qu'un "signal déclencheur" précoce mette en branle une séquence stéréotypée de synthèses métaboliques. Des études de localisation en fonction du temps, de BaP tritié ont montré que la fixation du traceur passait par un maximum, au niveau du foie, entre la 4 ème et la 6 ème hr après l'injection,[3] tandis que l'accroissement des activtés enzymatiques se manifeste déjà après 6 hr.[1]

On sait par ailleurs que certains types d'induction enzymatique sont radiosensibles, pour une dose déterminée de rayonnements et pour autant que l'irradiation affecte un horaire précis;[4] dans certains cas l'induction par substrat parait modifiée sous l'effet de l'irradiation immédiate[5] et la capacité de répondre à l'induction est déprimée à la suite d'irradiations reçues dans le jeune âge.[6] Comme ces divers types d'induction enzymatique semblent répondre à des modèles différents nous avons voulu