International Journal of Latest Research in Science and Technology **ISSN (Online):2278-5299**
Volume 8, Issue1: Page No. 5 - 7 , January – February, 2019
https://www.mnkpublication.com/journal/ijlrst/index.php

DOI: 10.29111/ijlrst-2019-10964

NEUROTOXICOLOGICAL EFFECT OF STEROIDAL DERIVATIVES IN CHANGES OF CHOLESTEROL LEVEL IN DIFFERENT REGIONS OF ALBINO RAT BRAIN

Sheeba Shafi
College of Applied Medical Science , King Faisal University Hofuf-Al-Hassa , 400, Saudi Arabia
sheeba@kfu.edu.sa

Abstract*: *Changes in the level of cholesterol in albino rat brain (Cerebrum hemisphere , Cerebellum and brain stem were evaluated following the administration of four steroidal derivatives as 3β-acetoxy-5-bromo-6β-Hydoxy-5α cholestane A(I), 3β-Acetoxy-6-dimethyl amino cholest -5-ene B (II), 3β-Chloro –5-bromo-6 β-nitro-5α-cholestane C (III) and 6 β-Amino pyrimidino-cholest-4 -ene -3-one D (IV).Experiments were carried out on four groups of six male albino rat weight 200 ± 20 g. Controlled rats were administered normal saline water intraperitonially (i.p) while the other experimental group were given 0.3 mg/ kg body weight of steroidal solution ,which was prepared in the peanut oil .

Keywords – cholesterol, cerebrum, cerebellum and brain stem

I. INTRODUCTION

Cholesterol is a major and the only sterol present in significant amount in the central nervous system[1]. Membranes are generally thought to consist of phospho lipid bi layer in to which membranes proteins are embedded. Yet cholesterol molecules are present in the most animal structure. Due to its amphipathic nature bearing an OH group and a hydrocarbon skeleton with rigid rings and branched chain of eight carbons. Cholesterol is perfectly suited to mesh with lipid bilayer[2] .Cholesterol account for about 10 % of dry weight of the brain as compared to less than 1% found in many others organs.

Steroidal drugs has been used for the wide range of diseases such as antiviral[3], antiallergic[4], anticonvulsant[5], antiulcer[6], analgesic[7] ,antifungal[3] , antihypertensive[5], antifertility[8], nerve exciting[9] ,anti bacterial[10] , anti fungicidal[10], anti thyroid[11,12,13], growth inhibitor[14],cardiac diseases[15] , skin disorders and as inflammation inhibitors[16]. At present steroidal drugs are the only drugs, which falls under the category of life saving drugs. These drugs are used daily in the highest medical emergency to save the life of millions of sufferer .Steroidal drugs are commonly used on the occasion , where any other non steroidal drugs generally failed to produce any curable effects.

However no systematic work on structure activity correlation is done so far on the various homologues of cholesterol on the brain. Earlier Islam et al[68] has studied the effect of estrogen and primovlar having slight difference in the structure on cholesterol level in the estrogen treated rabbit. It shows regional heterogeneity in exhibiting a depletion in the brain stem, spinal cord and increase in the cholesterol level in the cerebellum following 30 days administration. Primovlar treated rabbit shows the depletion of cholesterol level in hippo campus, amygdaloid nucleus , mid line nuclei of thalamus and gyrus cinguli in his study[17]. Islam also noted the alteration of cholesterol level was only significant after 90 days of administration.

II. MATERIALS AND METHODS

A lot of research work has been done in the field of hetero-steroidal synthesis .Their identification has been done by chemical and spectral studies [5,18,19].We have also synthesized a number of hetero-steroids in the cholestane series containing nitrogen, oxygen,sulphur and halogen, keeping in mind that they may be biologically active. We have studied the effect of following steroidal compound on the brains of rats which we have synthesized. The compounds are 3β-acetoxy-5-bromo-6β-hydroxy-5α cholestane A(I), 3β-Acetoxy-6-dimethyl amino cholest-–5-ene B (II), 3β-Chloro -5-bromo-6 β-nitro-5α-cholestane C (III) and 6β -Amino pyrimidino-cholest-4-ene-3-one D (IV).

The present study was undertaken to evaluate the neurotoxic effects of these steroidal compounds in lipid metabolism All these compounds were daily administered intraperitoneally (ip), 0.3 mg /kg body weight for ten days to a group of male albino rats.

Statistical analysis

Cholesterol was estimated according to the method of Zlatis et al. Table 1 shows the effect of steroidal derivatives in the content of cholesterol in cerebrum , cerebellum, and brain stem of rat .

Publication History
Manuscript Received : 13 February 2019
Manuscript Accepted : 19 February 2019
Revision Received : 26 February 2019
Manuscript Published : 28 February 2019

III. RESULTS

Table-1shows that 6β-amino pyrimidino-cholest-4-ene-3-one D (IV) produces most significant increase 460 % in

cerebellum while significant decrease is observed –112.2 % of cerebrum and 14.13 % in brain stem.

3β-Chloro-5-bromo-6 β-nitro-5α-cholestane C(III) shows significant decrease –361.9 % in the concentration of

cholesterol in cerebellum and –57.3 & in the cerebrum while it produces an insignificant deprivation in brain

stem -14.12 %.

3β-Acetoxy-6-dimerthylamino-cholest–5-ene B(II)produces significant decrease –89.7 %in cerebrum , -57.8 %

in brain stem and –51.9 % in the concentration of cholesterol of cerebellum .

3β-acetoxy-5-bromo-6β -Hydoxy-5α cholestane A (I)produces significant decrease in the cholesterol level in

Cerebrum (-81.8%) in cerebellum (-73.9 %) and in brain stem –32.9 %

Parameter	Brain region	Control (Average)	Experimental Structure –Activity - Correlation							
			A	% change	B	% change	C	% change	D	% change
Cholesterol	Cerebrum	0.0149	*** 0.0148	-81..8	*** 0.0152	-89..7	*** 0.0150	-57..3	*** 0.0146	-112..2
	Cerebellum	0.0023	*** 0.0023	-73..9	*** 0.0027	-51..9	*** 0.0021	-36,1..9	*** 0.0020	460.0
	Brain stem	0.0089	*** 0.0088	-32..95	*** 0.0090	-57..8	NS 0.0085	-14..12	NS 0.0092	14..13

IV. DISCUSSION

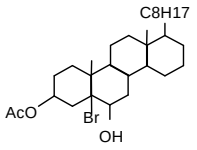
Regional alteration in the levels of cholesterol following the administration of 3β –acetoxy-5-bromo-6β -hydroxy -5α cholestane A(I), 3β–Acetoxy-6-dimethyl amino cholest –5-ene B (II), 3β-Chloro –5-bromo-6 β-nitro-5α-cholestane C (III) and 6β -Amino pyrimidino -cholest-4-ene-3-one D (IV), 3mg/kg body weight ip for 10 days in different regions of rat brain. We have estimated the changes in cholesterol level in major three regions of brain cerebrum, cerebellum and brain stem.

In the present study effect of the four derivatives were evaluated in the brain of albino rats. Activity of these steroids in the cerebrum is as follows. Four of these steroidal derivatives A(I), B(II) , C (III) and D (IV) gives significant decrease in the cholesterol level, among these B (II) gives -89.5%, C (III)-57.3%, A (I) -81.8% and D (IV) -119.2% in cerebrum. In the cerebellum compound D(IV) gives the most significant increase of 460.0% while compound B(II and A (I) gives significant decrease of -51.9% and 73.9% respectively, whereas compound C (III) gives 361.9% significant decrease in cholesterol level.

In the brain stem activity of compound B (II) and A (I) gives significant decrease in cholesterol level -57.8% and -32.95% while compound C (III) and D (IV) gives the insignificant decrease and increase of -14.12 % and 14.13 % respectively in cholesterol level.

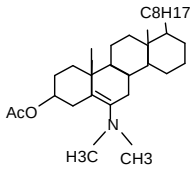
Analysis of the effect of compound A(I) on all the three brain parts reveals its maximum effect on cerebrum(-81.8% than cerebellum (-73.9 %) a significant decrease and less effective on brain stem is of -32.95%. Analysis of the effect of compound B(II) on different parts of the brain reveals its maximum effect on cerebrum (-89.50%)than brain stem (-57.80%) and then in cerebellum (-51.9%), its shows significant decrease on all parameters. The activities of compound C (III) on these three brain parts reveals its most significant decrease of -361.9% on cerebellum and then in cerebrum (-57.3 %) is of significant decrease where as insignificant decrease in the cholesterol level in cerebellum (-14.12%) is reported in this study.

Analysis of the effect of compound D(IV) on three brain parts reveal its most significant increase of 460% on cerebellum were as significant decrease on cerebrum (-119.2%) and on brain stem (14.13 %) in the cholesterol level is reported.



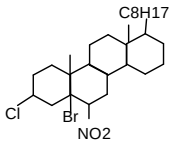
3β-Aceloxy-5-bromo 6 β-hydroxy. 5α-cholestane(A)

(I)



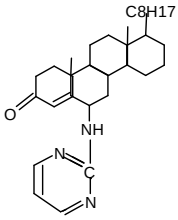
3β-Acetoxy-6-dimethylamino cholest-5-ene (B)

(II)



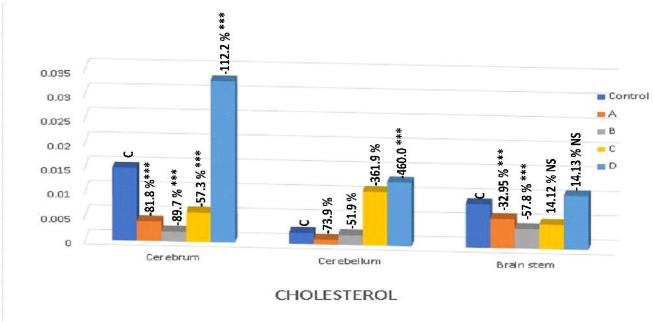
3β-Chloro-5-bromo,6 β-nitro-5 α-cholestane (C)

(III)



6β-Aminopyrimidino-cholest-4en-3one (D)

(IV)



V. CONCLUSION

Comparative study related to all four derivatives reveal that steroidal derivative compound D (IV) exerts its most

significant rise on cerebellum (460%) & induced depletion in the cholesterol level. Compound C (III) induces most significant decreases on cerebellum of -361.9 % & gives significant depletion in cerebrum and insignificant depletion on brain stem of –14.12& is reported. Compound B(II) induces maximum significant decreases in cerebrum , cerebellum and brain stem Compound A (I) induces maximum depletion on cerebrum, cerebellum and brain stem.

ACKNOWLEDGMENT

Author is thankful to Interdisciplinary brain research center (IBRC),Jawaharlal Nehru Medical college (J.N.M.C) AMU,Aligarh for their extensive support in conducting biochemical part of this work with in defined period of time. I am also thankful to Dr.E.H.Khan, a industry leader for his technical support.

Source of funding

No source of funding in any form has been received.

Conflicts of interest

There is no no conflicts of interest to declare in association with this paper.

REFERENCES

[1] Ansell G. B and J. N. Hawthrone, "Phospholipids, Metabolism and function", Elsevier, Amsterdam; 1964.

[2] A. Birgit, A. Stefan and E. Klas, Proc. Int. Rapessed Conf 5* 1978 Chem. Abstr; 92, 141499

[3] Awasthi L. P, S. P. Singh and Zentralbl, Microbiol; (1982), 137, 503

[4] Honma,Y. Sekine,T. Hashiyama, M. Takeda, Y. One and K.Tsuzurahara, Chem. Pharm. Bull (1982) 30, 4314

[5] Ahmad I and J. S. Shukla, Indian J. Physiol. Pharmacol; (1982). 26, 289 (Chem. Abstr; (1983)). 98, 154905

[6] Otsuka pharmaceutical Co Ltd; (JP82-980), Chem. Abstr; (1982), 97, 72370

[7] Foguet A. R, H. J. A. Ortiz, F. E. Fome and C. M. M. Raga, Chem.Abstr; (1983), 99, 5634

[8] Takeuchi M , I. Yokoi and M. Kurono, Neuropharmacology; (1977),16, 849

[9] Saito N, K. Hatakeda S. Ito, T. Asano and T. Todo, Bull. Chem. Soc;Jpn, (1986),59, 1629

[10] Grudzinski S, J. Ropenga, U. Zalega and H. Gniadek, Chem. Abstr; (1979),91,140835.

[11] I. Shibata, A. Baba and H. Matsuda, J. Chem. Soc, Chem. Commun; (1986), 1703

[12] Birgit A. Stefan and E. Klas, Proc. Int. Rapessed Conf 5* 1978 Chem. Abstr; (1980) ,92, 141499.

[13] Manfred W, S. Gerd and P. Kurt, Ger [East] DD2, 17, 806. Chem.Abstr; (1985), 104, 18618 (1985). [East] DD2, 17, 526, Chem.Abstr; 104, 186727

[14] A. Klaus, L. Henry, H. Helmet W. Rudolf and J. Michall, Ger. Offen,DE3,401, 680 Chem.Abstr (1985)104, 186719

[15] Islam F , M. Hasan, R. Rizvi and S.M. Osman, "Microanalysis of lipids in discrete brain areas of the rabbit following intramuscular administration of steroids contraceptive", Contraception; 4, 21

[16] Mushfiq M and N. Iqbal, J. Chem. Research(s); (1986) 224.