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REVIEW: ANTICONVULGENT ACTIVITY OF SOME NOVEL QUINOLONES DERIVATIVES

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ABSTRACT
The present study deals with the synthesis and anticonvulgent evaluation of a series of quinolone derivatives. Evolution of several kind of disease has proved that there is lots of opportunity to modify the potent molecules and develop new drugs. Quinolone derivatives are selective glycine site antagonists related to several central nervous system disorders including schizophrenia, Parkinson's disease, stroke, epilepsy and Alzheimer's disease.[1] A new series of substituted quinolone derivatives were designed and synthesized to meet the structural requirements essential for anticonvulsant properties.

KEYWORDS: Epilepsy, quinolone, glutamate receptor.

INTRODUCTION

Epilepsy is a syndrome, not a disease.[2] It is characterized by epileptic seizures, which are evoked by unexpected, high-level neuronal discharges in the brain[3]. These seizures are transient signs and/or symptoms of abnormal, excessive or hyper synchronous neuronal activity in the brain. 'A sudden, involuntary, time-limited alteration in behaviour, motor activity, autonomic function, consciousness, or sensation, attended by an abnormal electro-graphic pattern (EEG).[4]

Epilepsyis as old as time. Prehistoric man most like petitioned from the condition; evidence of trephining (drilling holes in the skull to cure neurological disorders) has been found among fossilized bones.[5]

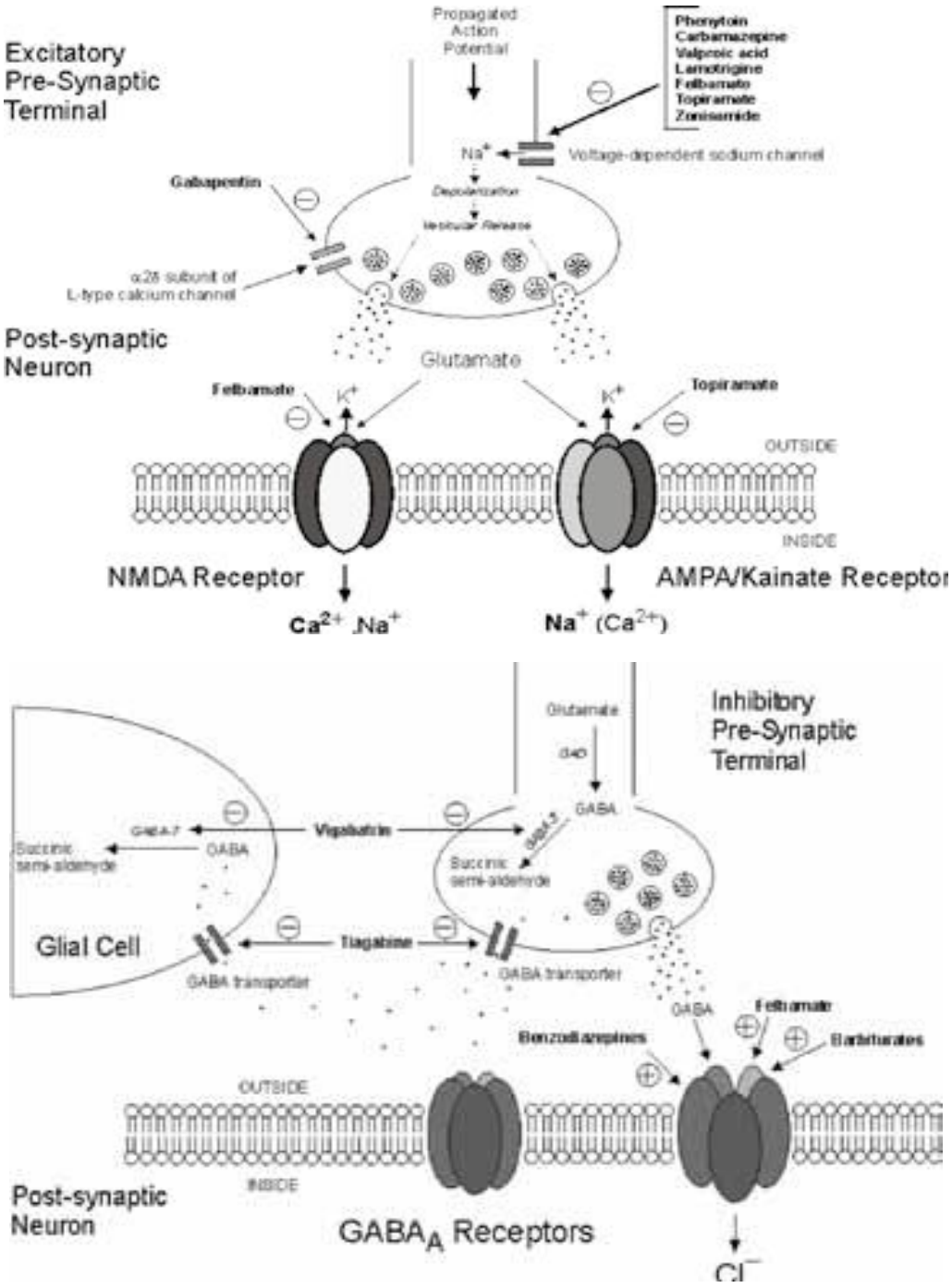
Uncontrolled epileptic seizures can be pernicious to a person's physical, mental and emotional health, social interactions, educational and vocational opportunities and quality of life. Antiseizure drugs available today can control the seizures in only 80% of the patients. These drugs have unfavourable side effects like sedation, ataxia, meglaloblastic anemia, GIT disturbances, weight loss and weight gain.[6]

Clinically used antiepileptic agents act by inducing protract inactivation of the Na^+ channels, by blocking Ca^{2+} channels or by enhancing inhibitory GABA ergic neurotransmission.[7]

Design of this work is based upon literature review of quinolone ring showing virile anticonvulsant activity. Epilepsy is usually controlled, but not cured, with speculation. However, over 30% of people with epilepsy do not have seizure control, even with the best available speculation. Surgery may be considered in difficult cases. Not all epilepsy syndromes are life-long; some forms are confined to particular stages of childhood (Surgery for seizures NEJM 1996).

MECHANISM OF QUINOLONE

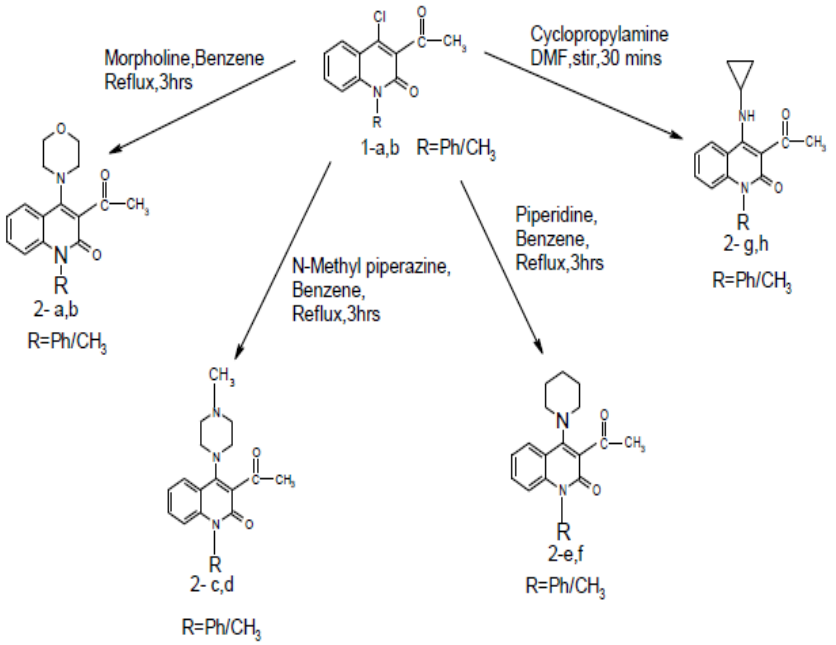
The primary mechanisms of action for these drugs take decreasing the excitation of neurons by blocking sodium and/or calcium channels or antagonizing glutamate receptors. Some medications increase the inhibition of neurons by increasing or enhancing γ-amino butyric acid (GABA).[8]



Both above figures are adopted from Rho JM, Sankar R. 'The pharmacologic basis of antiepileptic drug action.[9]

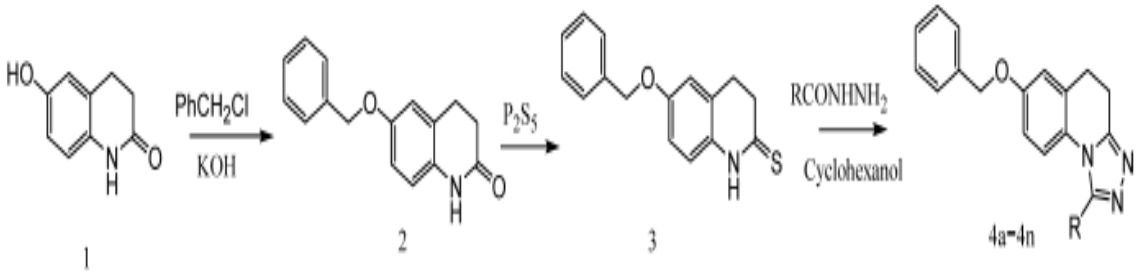
SYNTHESIS OF QUINOLONES AS ANTICONVELGENT MOLECULES

Sathe Vaishali and co-workers[10] synthesised 4-substituted-2-quinolone derivatives (2a-2h) as anticonvulsant agents by reaction of 3-acety-4-chloro-l-phenyl/ methyl quinoline-2(1H)-one with different primary and secondary amines.



Healthy young albino mice of either sex weighing 20 to 30 gms were used for acute toxicity study to determine LD50 value of various compound and for assessing anticonvulsant activity. Results were tabulated using one-way ANOVA and Dennett's't' test. 2a ($C_{21}H_{20}N_2O_3$), 2e ($C_{22}H_{22}N_2O_2$), 2h ($C_{15}H_{15}N_2O_2$) have shown promising and potent activity when compared with phenytoin as standard drug.

Li-Jing CUI, Zhi-Feng and his co-workers[11] synthesized 1-Substituted-7-Benzyloxy-4,5- dihydro-[1,2,4]triazolo[4,3-a] quinoline by refluxing 6-Benzyloxy-3,4-dihydro-1H-quinoline-2-thione with suitable acylhydrazine, and cyclohexanol.



a = H

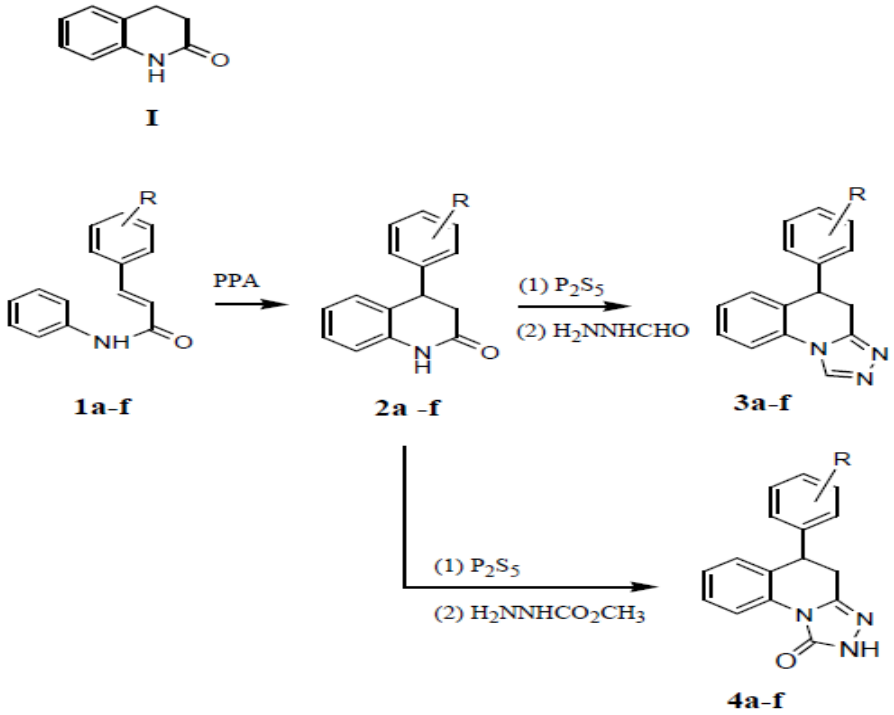
Compound 4a was the most active among the 14 compounds synthesized, with an ED50 value of 17.3 mg· kg1 in the MES test. Its activity was more potent than that of valproate (ED50272 mg· kg ¯1), comparable to that of Phenobarbital (ED50=21.8 mg· kg ¯1), and less effective than that of phenytoin (ED50= 9.5 mg· kg^{-1}).

Guan and his co-workers[12] synthesized a new series of substituted quinoline-2(1H)-one and 1, 2, 4-triazolo [4, 3-a] quinoline derivatives. Their anticonvulsant activities were evaluated by MES test, sc-PTZ test and rotarod test. Compound 7 showed the strongest anticonvulsant effect with ED50 of 27.4 mg/kg and 22.0 mg/kg in the anti-MES and anti-PTZ test, respectively.

Wei and his co-workers[13] synthesized a series of 2-substituted-7-heptyloxy-4,5-dihydro-[1,2,4]triazolo[4,3-a]-quinolin-1(2H)-ones and evaluated their anticonvulsant activities. Pharmacological tests showed that compound 6 was the most active and had the lowest toxicity (Table 1). In the anti-MES test, it showed ED50 of 8.2 mg/kg, TD50 of 318.3 mg/kg, and PI of 39.0, which was much greater than the PI of the reference drugs phenytoin and carbamazepine.

Li-Ping Guan and his co- workers[14] synthesised quinolone derivatives 5- substituted-phenyl-4,5-dihydro-1,2,4-triazolo[4,3- a]quinoline-1(2H)-one((4a-f) by incorporating a triazole or triazolone ring into N1-C2 positions of compounds2a-f. compound 4g with a TD50 value of greater than 300 mg· kg1, ED50 of 23.0 mg·

kg1 and protective index (PITD50/ED50) of more than 13 was the safest among the compounds synthesized. Compared with the marketed drugs, its ED50 value was comparable to that of phenobarbital in the MES test but its PI value was higher than that of phenytoin, carbamazepine, phenobarbital and valproate.



CONCLUSION

The extensive work reviewed here may represent a starting point to allow a better understanding of antiepileptic therapeutic developments as well as to suggest ideas on design and synthesis of novel antiepileptic compounds.

REFERENCE

1. McQuaid, L.A., Smith, E. C.; Lodge, D.; Pralong, P. J. J. Med. Chem., 1992; 35: 3423.
2. Thirumurgan R, Sriram D, Saxena A, Stables A, Yogeeswari P. Bioorg Med Chem., 2006; 14: 3106-3112.
3. Loscher W., Eur. J. Pharmacol, 1998; 342: 1-13.
4. Thompson, N., C, I. Osorio, Perspectives in Psychiatric Care, 2005; 41(2): 71 - 78.
5. Owsei Temkin, the Johns Hopkins University Press 1994(1945).
6. J. Chen, X.Y. Sun, K.Y.Chai, J.S. Lee, M.S. Song and Z.S.Quan, Bioorg. Med. Chem. 2007; 15: 6775-6781.
7. B.S. Meldrum, A.G. Chapman. Adv. Neurol., 1999; 79: 7-61.
8. Perucca E. Epilepsia, 2005; 46(4): 31–7.
9. Rho JM, Sankar R., Epilepsia 1999; 49: 1471–83.
10. Sathe Vaishali *, Vilegave Kailash1, Chandankar Pratibha2, International Journal of Pharmacy and Pharmaceutical Science Research 2012; 2(3): 45-49.
11. Li-Jing CUI, *a* Zhi-Feng XIE, *a* Hu-Ri PIAO, Biol. Pharm. Bull., 2005; 28(7): 1216-1220.
12. Guan, L.P.; Jin, Q.H.; Tian, G.R.; Chai, K.Y.; Quan, Z.S. J. Pharm. Pharm. Sci. 2007; 10: 254–256.
13. Wei, C.X.; Li, F.N.; Zhao, L.X.; Zhao, L.M.; Quan, Z.S. Arch. Pharm., 2007; 340: 491–495.
14. Li-Jing CUI, a Zhi-Feng XIE, a Hu-Ri PIAO, a Gao LI, a Kyu-Yun CHAI, b and Zhe-Shan QUAN* Biol. Pharm. Bull., 2005; 28(7): 1216-1220.