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THE ANTI-EPILECTIC/ANTI-CONVULSIVE EFFECTS OF MUSTARD SEED EXTRACTS.

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ABSTRACT

This research work investigated the anti-epileptic/anti-convulsive properties of ethanol, chloroform and water extracts of brown mustard seed *(Brassica junced)* on penicillin-induced epileptic rabbits. The levels of plasma glucose, creatinine and calcium ions were measured before, during and after convulsive feats as indices of the effects of the extracts on convulsion. The mean values of serum glucose before, during and after convulsion were 102.90mg/100ml, 59.37mg/100ml and 80.51mg/100ml respectively. Those of creatinine were 4.11mmol/l, 4.1ImmoL/l and 4.11mmol/l respectively, while calcium ion level; before, during and after convulsive feats were 10.20mg/100ml, 6.5mg/100ml and 9.06mg/100ml respectively. The greatest efficacy was observed in animals treated with water extracts, followed by ethanol and the least was chloroform. The level of creatinine did not change within the period, and suggested that the muscular contractions did not exhaust all the available glucose (immediate source of ATP) during convulsive feats. All mustard seed extracts were found to have anti-convulsive effects.

KEYWORDS: Anti-epileptic/anti-convulsive properties of ethanol, *Brassica junced.*

INTRODUCTION

Epilepsy is neurological condition that makes people susceptible to seizure (Singh et al., 1998). It is one of the most common neurological diseases known and about 1% of the world population suffers epileptic seizures yearly (Eric et al., 1982).

However, a seizure is a charge in sensation, awareness, or behaviour brought about by a brief electrical disturbance in the brain. It is an epileptic events and it's an outward sign of malfunction in the electrical system that controls the brain (Baulac et al., 2001). Seizure varies from momentary disruption of senses, short periods of unconscious less or staring spells, to convulsions (Charlier et al., 1998). Some have just one type of seizure while others have more than one type (Wang, et a], 1998). The major types being partial and generalized seizure.

Furthermore, a seizure can have many causes such as high fever, lack of oxygen (anoxia) poisoning (anoxia) many other factors such as over dosage of penicillin crystal, Nicotine, cocaine and amphetamine as well as infections, metabolic derangements, trauma, ischemia and tumor (Eric et al., 1982).

Besides, epileptic seizures can be classified based on clinical events, electroencephalograph characteristics, etiology, pathophysiology, anatomy or age (Walter et al., 2000). According to this, international League Against Epilepsy (1LAE) epilepsy is classified into two major groups, which include partial and generalized seizurie ss in which subclasses are located.

However, the investigations on the mechanisms of epileptic activities are beginning to address the interplay of the intrinsic electrical properties of the neurons against a background of the activity of the cell population (Walter et al., 2000). The electrical behariour of the cells, which is central to the normal, as well as the abnormal activities of the neurons, depends on ion conductance, primarily sodium ions, (Na^+ > calcium ions (Ca^{2+}), potassium ions (K^+) and chloride ions (Cl").

The ions conductance depends on the intra and extra cellular concentrations of these ions as well as the ioni; flux across the cell membranes. Ion flux across membranes is controlled by the combination of energy-dependent pumps; voltage-gated channels and n surotransmitter-controlied channels (Walter et al., 2000). This mechanism is centred on the excitation and inhibition of neurotransmitters, which affect the transmission of nerve impulses (William et al, 1995). In the same vein, the enzyme that catalyses the destruction of these neurotransmitters, also lead to epileptic

conditions if affected (Hole, 1981). On the other hand, the channels that regulate the movement of ions across the membranes, which lead to polariztoin and depolarization, have also been implicated in this mechanism to be the centre of epileptic control (Hole, 1981). In fact, if never impulses reach synaptic knobs at rapid rates, their supply of neurotransmitters may become exhausted, so that impulse cannot be transferred between neurons involved until more neurotransmitters are synthesized and this is what occurs during an epileptic seizure (Hole, 1981). In this situation an abnormal and excessive discharges of impulses originating from certain brain cells, reach skeletal muscle fibres and stimulate violent contractions seen in epileptic conditions (Hole, 1981). Consequently, the synaptic knobs seem to run out of neurotransmitters and the seizure begins (Hole, 1981).

Epilepsy is not a chronic disease. Many drugs have been developed and used in treatment of epilepsy. The fir it epileptic drug was bromide, which was used in the late 19 century but it side effects made it an unsuitable medication (Lossin et al., 2002). In 1912, Pher.obarbital became the main drug prescribed for epileptic patients and is still used today (Lossin et al., 2002). However, its usefulness was limited to generalized tonic-clonic seizure and to a lesser degree, simple and complex partial seizures but no effect on the absence seizure (Lossin et al., 2002). Many other synthetic drugs such as diphenylhydantoin, tridione, *;arbamazepine, valproic acid and felbamate were invented later in the century (Lossin et al., 2002). However, epilepsy is not only treated with synthetic drug Plants, herbs and spices that contain active chemicals are also used to cure an epileptic seizure. A typical example of such plant is rnus ard seed, which has been revealed experimentally to contain such chemicals that are capable of curing diseases.

It has been shown that mustard seeds are not only used to treat epilepsy but are important also in the treatment of microbial infections, disorders of digestive organs, snake poison, rheumatism, scorpion sting, cancer, etc (Steven, 2000). There are many species of mustard seeds, the black mustard seeds *(Brassica nigra)* which has the highest medicinal value, the brown mustard seed (*Brassica juncea)* and white *{Brassica alba}* which are also effective medicine .

AIMS

This project work is aimed at determining the anti-epileptic anti-convulsive properties of mustard seed extracts and their routes of administration.

EXPERIMENTAL ANIMAL **AND SEED FOR EXTRACTION**

- 7 Rabbits obtained from Ogbete main market Enugu, Nigeria.

• 200g of mustard seed obtained at St. Theresa Catholic Cathedral canteen, Ogoja Road Abakaliki.

METHODS

DESIGNATION *OS* ANIMALS

- Rabbit A = control i.e. without epileptic inducer and no treatment. « Rabbit B = Negative control i.e. infected with epileptic inducer, without being treated with any of the extracts.
- Rabbit C = induced and treated orally with 5ml of extract for 3 days and 3 times daily.
- Rabbit D= Induced and treated intravenously with 0.5ml of the water extract for 3 days and J times daily.
- Rabbit E = induced and treated intravenously with 1ml of the water extract for 3 days and 3 times daily.
- Rabbit F= induced and treated orally with 3ml of ethanol extract for 3days and 3 times daily.
- Rabbit G= induced and treated orally with 3ml of chloroform extract for 3days and 3 times daily.

PREPARATION OF REA GENTS

- 100mg/1 of standard calcium solution was prepared by dissolving O.Olg calcium in 100ml of distilled water.
- 4% ammonium oxahte was prepared by dissolving 4g of ammonium oxalate in 100ml of distilled water.
- 0.5M of $H_2SC>4$ was prepared by pipetting 2.7ml of stock $H_2SC>4$ into 100ml of distilled water.
- 0.01M of KMnO4 was prepared by dissolving 0.15g of $KMnO_4$ in 100ml of distilled water.
- 2% ammonium solalion was prepared by pipetting 2ml of the stock ammonium solution into 98ml of distilled water. » 5% sodium tungsta;e was prepared by dissolving 5g of sodium tungstate in 100ml of distilled water.
- 0.75M NaOH was prepared by dissolving 3g of NaOH in 100ml of distilled water.
- 0.33M of H2SC>4 was prepared by pipetting 1.8ml of H2SO4 stock into 100ml of distilled watsr.$_p$
- 20rng/ml of creatin; ne standard was prepared by dissolving 2g creatinine in 100ml of distilled water.
- Solution 1 consist 85mmol/l sodium sulphate and 24mmol/I of copper sulphate.
- Solution 2 is 272mmo/l of sodium tungstate.

- Solution 3 is 52mmol/l of copper sulphate, 0.60mmol/l of sodium bicarbonate, 0.38mmol/l of sodium carbonate, 0.02mmol/l of potassium oxalate and 0.09mmol 1 of Rochelle reagent.

* Solution 4 is Glucose standard.
* Solution 5 is Arsenomolybdate reagent l.e 40mmol/l ammonium molybdate, 0.79mmol/l of H_2SO_4 and 19mmol/l of sodium Arsenate.

EXTRACTION

200g of mustard seed was grcund, after grinding, it weighed 189.4g and 80g of the powdered mustard seed was transferred to 200ml of distilled water.

The mixture was allowed to stand for 24hours at room temperature. After 24hours the mixture was filtered and the filtrate or aqueous extract kept in fridge after each day of treatment.. Ethanol extract was prepared by transferring 40g of the ground mustard seed to 100ml of ethanol The mixture was allowed to stand for 24hours in a room temperature. After 24hours the mixture was filtered and the filtrate exposed in open air for 1 hour and then kept in fridge after each day of treatment. Chloroform extract was prepared by transferring 40g of the ground mustard seed to 100ml of chloroform. The mixture was allowed to stand for 24hours in room temperature, after 24hours the mixture was filtered and the filtrate exposed in open air for I hour and then kept after each day of treatment.

ESTIMATION OF PLASMA CALCIUM ION CONCENTRATION

2ml of the plasma and 1ml of standard calcium solution were pipetted into a test tube. Into another test tube, 2ml oi'distilled water and 1ml of standard calcium were mixed which served as control or blank. After which, 2ml of distilled water and 1ml of 4% ammonium oxalate were added to each test tube and were properly mixed and allowed t :> stand for 1 hour with shaking at regular interval (10 mins). The solution was filtered and the precipitate washed twice with 3ml portion of 2% ammonia solution. The filter paper and the precipitate were carefully transferred into 25CmI conical flask, and 10ml of 0.5M $H2SO_4$ and 50ml of distilled water were added and heated to almost boiling. The hot solution and the filter paper were titrated with 0.01M KMnO4 to a faint pink end point.

Using the blank containing 10ml of 0.5M $H2SO_4$ and 50ml of distilled water, which was heated as the sample. The whole processes were repeated for the remaining 6 rabbits, for 5days. i.e.before some rabbits were induced, after induction and 3days of treatment.

ESTIMATION OF PLASMA CREATININE

0.5ml of plasma was placed in a test tube and 0.5ml of distilled water was added and mixed. 1ml of 5% sodium tungstate and 1ml of 0.33M H_2SO_4 were added and properly mixed, which was allowed to stand for 5mins. After which, it was filtered.

1.5ml of protein free filtrate (PFF) was dilute with 50ml of distilled water and transferred to test tube labeled sample. 0.5ml of saturated picric acid and 0.5ml of 0.75M NaOH were added into the test tube.

It was mixed and allowed to stand for 15mins. The absorbance was read at 500nm using blank which contain 0.5ml of water, 0.5ml of picric acid and 0.5ml of 0.75MNaOH to zero the spectrophotometer. The absorbance of standard prepared by taking.0.75ml of standard creatinine, 0.75M NaOH which was allowed to stand for 15 minutes, was read at 500nm. This was done for the seven samples for 5days and the absorbance of the samples and standard, for each day were read.

1.85ml of solution 1 and 0.5ml of sample were pipetted into a test tube and mixed well. 0.1ml of solution 2 was added and shook thoroughly. The mixture was centrifuged at 3000 rpm for 5mins. Thereafter, 3 test tubes were set in a rack and labeled as follows:- Blank which contain 0.5ml cf distilled, standard (std) which contain 0.5ml of solution 4 and the test sample (t) containing 0.5ml supernatant of the centrifuged mixture. Then 0.5ml of solution 3 was pipetted into each of the test tubes and mixed well. I.e into the blank, std and t. These test tubes were covered with non-adsorbent cotton wool and boil for 10 minutes in water bath, which must be boiling before placing the test tubes. After the mentioned minutes, they were immediately cooled in water. In each test tube 0.5ml of diluted solution 5 was added (dilution ratio of solution 5 and water=l:2). The mixtures in the test tubes were mixed and allowed to stand for 2mins. After 2mins, 2.5ml of distilled water was added to each test tube and well mixed. The absorbance of the sample (t), standard (std) were read at 680nm, using the blank to zero the spectrophotometer. The absorbance of samples, standard and the corresponding glucose level were recorded in chapter 4 for the 7 rabbits, for 5 days.

Calculation of seium glucose=(AT/AS)xl20mg/ 100ml or (AT/AS)x6.66mmol/l. AT=Absorption of test sample and AS-Absorption of standard. Normal range-7Q-I20mg/100ml or 3.3-7.4mmol/l

METHOD OF COLLECTING BLOOD SAMPLE

The blood samples were collected intravenously through vein in the ear. The samples that were used for glucose test quickly transferred to sample bottle containing fluoride oxalate / potassium oxalate.

RESULTS

TABLE I: PLASMA CALCIUM RESULT.

Table 1 above shows level calcium in the blood before, during induction.

AMINAL	TEST TITRB (ml)	BLANK TITRE (ml)	Ca^{2+} level (mg/lOOml)
Before induction			
RABBIT A	2.50	1.50	10.0
RABBIT B	2.60	1.50	11.0
RABBIT C	2,60	1.50	11.0
RABBIT D	2.55	1.50	10.5 -
RABBIT H	2.50	1.50	10.0
RABBIT F	2.55	1.50	10.5
RABBIT U	2.50	1.50	10.0
A Her induction			
RABBIT A	2.60	1.60	10.0
RABBIT B	2.30	1.60	7.0
RABBIT *C*	2.35	1.60	7.5
RABBIT D	2.20	1.60	6.0
RABBIT I<	2.20	1.60	6.0
RABBIT F	2.30	1.60	7.0
RABBIT G	2.20	1.60	6.0
I^{s} dav of treatment			
RABBIT A	2.60	1.60	10.0
RABBIT B	2.30	1.60	7.0
. RABBIT C	2.40	1.60	8.0
RABBIT D	2.45	1.60	8.5
RABBITK	2.50	1.60	9.0
RABBiTF	2.35	1.60	7.5
RABBIT G	2.30	1.60	7.0
2^{nt} day of treatment			
RABBIT A	2.60	1.60	10.0
RABBIT B	2.40	1.60	8.0
RABBIT C	2.55	1.60	9.5
RABBIT D	2.60	1.60	10.0
RABBIT Ii	2.60	1.60	10.0
RABBIT F	2.50	1.60	9.0
RABBIT G	2.40	1.60	8.0
3 days of trcalmcnl			
RABBIT A	2.60	1.60	10.0

RABBIT B	2.50	1.60	9.0
RABBIT C	2.65	1.60	10.5
RABBIT D	2.65	1.60	10.5
RABBIT I-	-	-	-
RABBIT F	2.55	1.60	9.5
RABBIT G	2.50	1.60	9.0

Table 2: CREATININE LEVEL RESULT

Table 2 above shows level ;reatinine in the blood before, during and after action.

1 AMINAL	Absorbance of std	Absorbance of sample	Creatinine level
1 Before induction			
1 RABBIT A	1.135	0.478	4.21
1 RABBIT B	1. 149	0.576	5.01
1 RABBIT C	1,327	0.490	3.70
IRABBITD	1. 135	0.479	4.22
J RABBIT E	1. 149	0.449	3.91
r RABBIT F	1. 149	0.483	4.20
RABBIT G	1.135	0.511	4.50
After induction			
RABBIT A	1.166	0.491	4.2 1
RABBIT B	1. 149	0.576	5.01
RABBIT C	1.327	0.491	3.70
RABBIT D	1.135	0.479	4.22
RABBIT E	1.149	0.449	3.91
RABBIT F	1.149	0.483	4.20
RABBIT G	1. 135	0.511	4.50
***1* day* of treatment**			
RABBIT A	1.166	0.491	4.21
RABBIT B	1.149	0.599	5.21
RABBIT C	1.327	0.490	3.70
RABBIT D	1,135	0.479	4.22
RABBIT E	IJ49 '	0.449	3-91
RABBIT F	1.149	0.483	4.20
RABBIT G	1.135	0.5 1 1	4,50
2'"[1] day of treatment			
RABBIT A	1.181	0.497	4.21
RABBITS	1.164	0.606	5.15
RABBIT *C*	1.342	0.497	3.70
RABBIT D	1.150	0.485	4.22
BABBIT E	1.164	0.455	3.91
RABBIT F	1.164	0.489	4.20
I RABBIT G	1.150	0.518	4.50
I: days of treatment			
• BABBIT A	1.152	0.485	4.21

•RABBITB	1.165	0.584	5.01
•RABBITC	1.328	0.491	3.70
•RABBIT D	1.289	0.544	4.22
•RABBITE	-	-	-
RABBIT F	1.165	0.489	4.20
RABBITG	1.289	0.580	4.50

TABLE 3: RESULT FOR GLUCOSE TEST

Table 3 above shows level glucose in the blood before, during and after induction.

1 AMINAL	Weight (kg)	Absorbance of std	Absorbance of sample	Glucose level(mg/100ml)
B Before induction				
RABBIT A	1 .200	0.016	0.019	101.05
RABBIT B	0.675	0.015	0.019	96.01
RABBIT C	1.350	0.017	0.019	107.40
RABBIT D	1.475	0.018	0.019	113.68
RABBIT E	1.300	0.016	0.019	101.05
RABBIT F	1.250	0.016	0.019	101.05
RABBIT G	1 . 1 80	0.016	0.019	101.05
After induction				
RABBIT A	-	0.016	0.019	101.05
RABBIT B	-	0.008	0.019	50.50
RABBIT C	-	0.009	0.019	56.84
RABBIT D	-	0.011	0.019	69.47
RABBIT E	-	0.009	0.019	56.84
•RABBIT'v	-	0.009	0.019	56.84
RABBIT G	--	0.009	0.019	56.84
1^{s} day of treatmcnl				
RABBIT A	-	0.017	0.020	102.00
RABBIT B	-	0.008	0.020	48.00
y RABBIT C	-	0.010	0.019	63.16
1 RABBIT D	-	0.013	0.019	82.11
1 RABBIT *E*	-	0.0 11	0.020	66.00
1 RABBIT F	-	0.010	0.019	63.16
1 RABBIT G	-	0.011	0.019	69.47
" 2nd day of treatment				
RABBIT A	-	0.016	0.019	101.05
RABBIT U	-	0.009	0.019	56.84
RABBIT C	-	0.012	0.019	75.79
RABBir D	-	0.015	0.019	94.74
i RABBIT E	-	0.014	0.019	88.42
RABBIT F	-	0.012	0.019	75.79
RABBIT G	-	0.012	0.019	75.79

i 3 days of treatment				**1**
RABBIT A	-	0.016	0.019	101.05
RABBIT B	-	0.010	0.019	63.16
RABBIT C	-	0.15	0.020	90.00
RABBIT D	-	0.17	0.020	102.00
RABBIT E	-	-	-	-
RABBIT F	-	0.014	0.019	88.42
RABBIT G	-	0,013	0.019	82.11

DISCUSSIONS

During the course of this research plasma calcium was found decreased after induction. This is in line with the work earlier research done on epilepsy. That the response of plasma calcium is usually negative, that is decrease in concentration of plasma calcium ion Ca^{+} and increase in the muscular calcium ion (Rewan et al., 1993). The reduction is caused by withdrawal of Ca^{2+} from the blood circulation to relief muscles contraction or spasm which is one of the physical characteristics of epiLepsy. It is important to note that Ca^{2+} is needed for the closure of the sodium channels in the nerve fibre. This channels constantly remain open during epilepsy and impulses continue to be transmitted which are seen as muscle firing. However, during the treatment, it was seen that the level of calcium ion was increasing progressively as the treatment continues. The rising shows that the abnormalities caused by the epileptic inducer are being corrected by this drug (mustard seed extract). Furthermore, there are differences in the rate of recovery which is proportional to the amount of drug that reaches the target cell.

Although, it was not exactly proportional to the dosage, recovery increases with dosage for intravenous administration. But for oral administrations, one should think that rabbit C, F and G will recover at highest rate, having been treated with the highest dose. But the reason is not far fetched, knowing that drug administered through this route undergoes biotransformation and only little quantity of the drug that reach the target (Hardman et al., 2001). And for extracts of organic solvents, they are also effective, but not as effective as that of water extract.

In addition, creatinine level h the plasma did not change significantly as was stated earlier in chapter two, that the level of plasma creatinine increases during epileptic feats (Norbent, 1986). This could be because there were other closer alternative sources of energy, which were still available in the system of the animals. The use of phosphocreatine, which is the precursor of creatinine, is said to take place when level of energy sources are depleted. This is generally observed in very active athletes and therefore it serves as energy butter (Nelson et al., 2000).

In fact this important energy buffer might only be utilized when several seizures have occurred, and other sources of energy being depleted. Besides, blood glucose level which was the third parameter assayed in this research was seen to decrease during the seizure. The reason being that a lot of energy is needed during epilepsy for the individual to remain conscious. It should be noted that individual with high muscular activities utilized more energy than a resting individual (Zubay et al., 1995). However other sources of energy such as glycogen, free fatty acid, glycerol and lactic acid may be utilized to provide ATP-when glucose is depleted. The presence of these compounds in the system of these rabbits may be the reason while there was no significant change of creatinine level. In fact, during the cause of this research we found out that change in the level of glucose after induction is inversely proportional to the weight of the rabbit. That is the higher the weight, the lesser the change of the glucose level.

And during treatment the rat; of increase or recovery was directly proportional to the amount of drug injected intravenously. But for rabbit C, F and G which were orally treated. They did not recover faster than rabbit E, even though they received the highest dose of the anti-epileptic drug (Mustard seed extracts).

Meanwhile, the reason could be that a very small quantity of the drug reached the target area due to biotransformation reaction.

In general, the experiment was not done without casualty. In fact, one of the rabbits, i.e rabbit E, died on the third day of treatment. The death could be as a result of blockage in some veins which may have deprived vital organs, an access to blood and important macromolecules. Secondly, the reduction in the blood and important macromolecules taken for this analysis without corresponding replacement could be be another cause.

CONCLUSION

Mustard seed having been used to correct epileptic feats, one should be in right position to say that it is an anti-epileptic agent or that it contains active chemicals that are capable of correcting neuronal disturbance or disorder that are responsible for the epilepsy. Thus it can be given to an epileptic patient.

However, levels of glucose and calcium where found to decrease after induction and progressively rise as the treatment with mustard seed extracts continued. But the level of creatinine was not affected after induction and during the treatment, showing that there are

other sources of energy that were still available for the cells.

Mustard seed is good to be taken as spices by epileptic and non-epileptic individuals especially heavy alcohol drinkers,so as to reduce the risk of having seizures. But care should be taken, not to eat it in high quantity. This is being in use, it has been implicated to cause goitre.

REFERENCES

1. Baulac, S., HuberfeId,G., Gourfmke!-An, I,, Mitropoulou, G., Beranger, A,, Prud'homme, J.F., Baulac, M,, Brice, A,, Bruzzone, R., LeGuern, E. (2001). First genetic evidence of GABA(A) receptor dysfunction in epilepsy: a mutation in the gamma2-subu;iit gene. National Genetics, 2001; 28; 46- 48.
2. Charlier, C.;Singh, N.A., Ryan, S.G,, Lewis, T.B., Reus, B.K, Leach, RJ, Leppert, M. (J998). A pore mutation in potassium channel gene in an idiopathic epilepsy family. National Genetics: 1.8: Pp. 53- 55.
3. Eric, R. K and Shwartz $_7$ J . H (1982). Principles of Neural Sciences, 2nd edition. Elsevier North Holland, Inc. New York: 1982, Pp. 271-290.
4. Hardman, JH. G, Limbird, L. E. and Goodman, A.G. The Pharmacological Basis of therapeutics. 10th edition. The McGraw Hill companies Inc, New York: 2001, Pp. 1894-1895.
5. Hole, W. J. Jr. Human Anthony and physiology, 2nd edition. Win. C. Brown company publishers: 1981, pp. 276-281.
6. Lossin, C. Wang, D.W., Rhodes ,T H., Vanoye, C.G., George, A.L. Jr. Molecular basis of an inherited epilepsy. Neuron: 2002; 34: 877- 884.
7. Nelson,D.L. and Cox, M.M.(2000(. Lehninger Principles ofBiochemistry, 3rd edition. Worth Publisher, New York. 2000; 233-239, 502, 875.
8. Nelson,N. Biological Cherristry, Sedition: 1944, Pp. .l53&375.
9. Norbent, W. T. Ciinica! Cherristry, Sedition. W.B. SaunderPublishing Company, USA: 1 986, Pp. 1271-1279,
10. Rewan, J. A; John, R. G. (1993). Non-epileptic seizures, 1st edition.
11. Singh, N.A., Charlier, C., Stauffer,D., DuPont, B.R., Leach ,R.J., Melis, R., Ronen, G.M., Bjerre, I, Quattlebauni,T,, Murphy, J.V., McHarg, M.L., Gagnon ,D., Resales, T.O., Peiffer ,A., Anderson, V.E.& Leppert, M.. A potassium channel gene, is mutated in a,i inherited epilepsy of newboms. National Genetics, 1998; 18: 25-29.
12. Walter, G. B.; Robert, B. D. Gera!d, M. F.& Madsen, C. D. Neurology in Clinical practice, 3rd edition. Buttenvorth-Heinemann publisher: 2000, pp. 426-473.

13. Wang, H.S., Pan, Z., Shi, W., Bro*n, B.S., Wymore, R.S., Cohen, I.S., Dixon, J.E. & McKinnon, D. potassium channel subunits: molecular coirelates of the M-channei. Science, 1998; 282 :1890-1893.
14. William, G. G. Medical physiology, 7th edition. Appliceton, Lange, Asimon and Schuster company. USA: 1995, Pp. 820 - 850,
15. Zubay, G.L., Parson, W.W.and V.mce, D.E. Principles of Biochemistry, 2nd edition. Wm.C.Brown Communication, Inc: 1995, Pp. 602-619.