Chapter 4

Biological Applications of Naphthalene based Quinoxaline Derivatives

4.1. Introduction

4.1.1. 5-HT$_3$ receptor antagonism used as neurotransmitter

New arrangement of fundamentally novel 3-substituted-2-carboxamides quinoxaline was outlined as 5-HT$_3$ receptor opponents utilizing ligand-based approach. Every one of the mixes combined displayed 5-HT$_3$ receptor hostility and some of them demonstrated threat more noteworthy than the standard medication, on dansetron, as [3-ethoxy quinoxalin-2-yl] [4-methyl]piperazin-1-yl]-methanone and N-[2-(1H-indol-3-yl) ethyl]-3-ethoxy quinoxaline-2-carboxamide. The compound N-3-methoxy quinoxalin - 2-carboxamide demonstrated the most positive 5-HT$_3$ receptor. Likewise 3-benzyl-2-substituted quinoxalines were orchestrated as novel monoamine oxidase A (MAO-An) inhibitors. The MAO inhibitors are exceptionally helpful for the treatment of a few neurological sicknesses, similar to Parkinson and misery. MAO-An inhibitors are utilized as energizer and antianxiety drugs [Radhakrishnan Mahesh, T. D. et al., 2011]. In this review, the last mixes were assessed for their MAO-An inhibitory action in vitro, utilizing serotonin as substrate [Patidar, A. et al., 2011].

5-Hydroxytryptamine (5HT), usually called as serotonin, is a neurotransmitter required in an extraordinary number of physiological and
patho-physiological procedures, acting through the receptor subtypes, from 5-HT\textsubscript{1} to 5-HT\textsubscript{7}. All of the receptors sub sorts have a place with the group of G-protein coupled receptor (GPCR), however the particular receptor subtype 5HT\textsubscript{3} is a ligand gated particle channel. The opponents to this receptor prompt different reactions, for example, hostile to emetic activity in growth chemo/radio-treatment incited nauseousness and heaving, energizer, anxiolytic, against phsyotic and against inflammator. In any case, the medications accessible to sorrow conditions have a deferred onset of activity, which stresses the request of new upper medications, with a more secure and speedier activity [Peroutka, S. J. et al., 1997].

4.1.2. Neuroprotective Therapies

Parkinson sickness (PD) was portrayed by a dynamic loss of dopamine (DA) neurons inside the substantia nigra (SN) and as a result by a diminishing in striatal DA, at the nerve terminal level [Dauer, W. et al., 2003]. The consumption in striatal DA represents the run of the mill engine side effects of the malady. In the present condition of learning, there is no solid answer about the instruments bringing on DA cell demise regardless of the possibility that few speculations have been advanced to clarify the sub-atomic premise of neuronal harm. Specifically, it has been proposed that mitochondrial brokenness, oxidative anxiety, calcium dyshomeostasis and neuroinflammatory forms including glial cells could all contribute effectively to DA cell death Drugs that supplant DA or initiate its receptors can cure
engine indications with viability, yet such medicines can't stop or even back off malady movement and they additionally incite reactions that wind up plainly discrediting [Quinn, N. P. et al., 1998]. Neuroprotective/neurorestorative treatments, which are as yet hypothetical in PD, depend on the idea that powerless DA neurons in the SN can somehow be shielded from the degenerative procedure that prompts their downfall. Those medicines ought to be, be that as it may, given as ahead of schedule as conceivable to be successful in PD patients, as engine indications show up when the eradication in DA cell bodies surpasses half [Kansara, S. et al., 2012].

### 4.1.3. Development of Neurotrophic Factor

Glial-cell inferred neurotrophic consider (GDNF) has been proposed as a helpful operator to postpone the improvement of PD [Lin, L. F. et al., 1993], but clinical trials have been frustrating, most likely because of inborn disadvantages related with the utilization of peptides connected as medications, including pleiotropic impacts, short half-life and powerlessness to cross the blood cerebrum obstruction (BBB), along these lines forcing rehashed transcranial infusions, with undesirable reactions [Yasuhara, T. et al., 2007, Barker, R. A. et al., 2006]. Substantial efforts have been made, therefore, to develop non-peptidic small molecules with protective/restorative activities for DA neurons [Saragovi, H. U. et al., 1991].
4.1.4. Protective Potential of Quinoxalines in DA Neurons.

If some of these compounds are known to provide protection against acute neuronal excitotoxic lesions [Long, S. K. et al., 1990, Kong, L. L. et al., 2006], as far as anyone is concerned the properties of quinoxalines have not yet been assessed altogether in an unending degenerative setting. We were intrigued, here, to portray the defensive capability of quinoxalines for DA neurons. Consequently, we outlined and combined some new substituted 6-aminoquinoxaline subsidiaries exploiting unique and very regioselective techniques for union that we created in house [Hui, X. et al., 2007]. To measure the activity of these compounds, we used midbrain cultures and different experimental settings that model the loss of DA neurons in PD [Michel, P. P. et al., 1990]. As far as anyone is concerned the properties of quinoxalines have not yet been assessed altogether in an unending degenerative setting. We were intrigued, here, to portray the defensive capability of quinoxalines for DA neurons. Consequently, we outlined and combined some new substituted 6-aminoquinoxaline subsidiaries exploiting unique and very regioselective techniques for union that we created in house.

4.1.5. Quinoxalines are Tested in Dying DA Neurons

MPAQ was the only quinoxaline derivative tested in this study that was protective for spontaneously dying DA neurons. This compound was characterized by the presence of an aromatic ring in position 3 of the quinoxaline core structure suggesting this chemical feature was crucial for
DA cell rescue. Noticeably, the other compound of interest in this study produced an increase in the uptake of DA neuron and also stimulated the morphological differentiation of DA neurons without influencing the rate of survival of these neurons. A disconnection between survival promotion and differentiation is rather unexpected, as MPAQ and more generally other neuritogenic molecules, including for instance GDNF, exert both effects.

More specifically, we used an original and highly regioselective method for the synthesis of 2,3-disubstituted 6- aminoquinoxalines, which was previously established in our laboratory [Hui, X. et al., 2007]. A screening approach allowed us to show that MPAQ (2methyl-3-phenyl-6-aminoquinoxaline, compound affords substantial protection in a culture system of DA cell death in which neuro degeneration occurs spontaneously and selectively as a consequence of a mechanism involving immature astrocytes and secondarily a deficit in calcium homeostasis [Toulorge, P. et al., 2010]. This explains why antimitotic agents such as cytarabine, which interfere directly with glial mechanisms and compounds, which stimulate neuronal excitability such as nicotine and the beevenom component apamin, were reported to provide substantial protection in this paradigm [Salthun-Lassalle, B. et al., 2004, Toulorge, D. et al., 2011], nicotine and apamin were also protective in animal models of the disease, which attests to the validity of this culture system and reinforce the interest of the present results obtained with MPAQ [Parain, K. et al., 2003, Alvarez-Fischer, D. et al., 2013].
4.2. Materials and methods

4.2.1. Animal subject used

Swiss albino mice of male gender (21–24 g) were used throughout the study. They were provided normal pellet diet and drinking water *ad libitum* and were exposed to 12 hours sunlight and 12 hours dark cycle. The animals were made physiologically responsive to the laboratory conditions prior to the experiments. Animals’ care was taken as per guidelines of the Committee for the Purpose of control and supervision of experiments on animals (CPCSEA), Environment and Forests Ministry, India.

4.2.2. Drugs Used

Diazepam hydrochloride (Ranbaxy Laboratories, Gurgaon, India) was procured and used as a standard drug and it was diluted with saline water to the needed strength prior to the use. The test compounds were suspended in 0.3% w/v of sodium carboxymethyl cellulose (CMC) and were administered through oral gavage.

4.2.3. Acute Toxicity Studies

Acute Oral Toxicity (AOT 423) guideline was followed for the acute toxicity studies of the synthesized compounds. Briefly, overnight fasted animals were treated with various concentrations of the compounds to be tested (5, 50, 300 and 2000 mg/kg, bw) by oral route. The observation of animals for any behavioral changes or mortality for first 24 hours was done.
The animals were maintained for another 14 days to check the abnormal changes and mortality. Based on the results, the dose was fixed for pharmacological studies.

4.2.4. Anxiolytic activity

4.2.4.1. Elevated plus Maze (EPM) Test

To assess the anti-anxiety activity of test compounds, elevated plus maze (EPM) was used. Two open arms (16 × 5 cm) and two closed arms (16 × 5 × 12 cm) having an open roof, with the plus-maze elevated (25 cm) from the floor was the set up. Each mouse was individually placed at the centre of the EPM with its head facing exactly the open arms. This experiment lasts 5 minutes, during which behavior of the mouse was recorded as: (a) the number of entries of drug into the open arms, (b) mean time spent by the mouse in the open arms (mean time or average time = total time spent in open arms/number of entries in arms).

Procedure

Animals were divided in to 11 groups, each 6 in a group. The Group I served as control served with vehicle, Group II served as standard served with diazepam at the dose of 0.5mg/kg. Group III - XI the animals were treated with the compounds to be tested at the dose of (5 mg/kg, bw, p.o). The compounds were administered through oral way using a tuberculin syringe fitted with oral canula. The drug administration schedule was adjusted so that
each mouse was having its turn on the EPM apparatus 45 minutes after the administration of the dose. During the complete experiment, all the animals were allowed to socialize. Every care was taken to make sure that no external stimuli, other than the height of plus-maze could invoke anxiety in the animals. The parameters noted is (a). Time spent in open arm and (b). Number of arm entries to assess the anxiolytic activity.

4.2.5. Sedative and Hypnotic activity

4.2.5.1. Hole - Board Test

In order to examine the sedative and hypnotic activity of the synthesized compounds, Hole-Board Test was performed. The hole-board apparatus is set to comprise a grey Perspex panel (40×40 cm, 2.2 cm thick) with 16 equidistant holes (diameter of 3 cm) in the floor. Photocells below the surface of the holes have given way for the measure of the number of head dips. The board was placed 15 cm above the table and it was divided with black water-resistant marker into 9 squares of 10×10 cm. 30 minutes after the introduction of the test drug; each mouse was separately placed in the centre of the board. During these 5 minutes of test period, number of head dips was observed.

Procedure

Animals were broadly divided in to eleven groups, each 6 in a group. The Group I served as control served with the vehicle, Group II served as
standard served with diazepam drug at the dose of 3 mg/kg. Group III - XI the animals were treated with the test compounds at the dose of (5 mg/kg, bw, p.o). The compounds to be tested were introduced orally using a tuberculin syringe fitted with oral canula. After 45 minutes of oral administration of the test compounds, the animals were placed in to the center of the perforated board and noted for the period of 5 min and the number of head exploration was counted in order to find out the sedative and hypnotic activity.

4.2.6. Locomotor activity

For the purpose of evaluating the spontaneous locomotor activity of the synthesized compounds, actophotometer was used. Actophotometer (24×22×10 cm) (Popular Traders, Ambala) with automatic counting of animal movements in the floor of activity cage was utilized for the present study. Mice were placed individually in activity cage for 5 minutes test period, 45 minutes after administration of test drugs. Locomotor activity was observed in terms of the activity scores.

Procedure

Animals were divided in to 11 groups, each group consists of 6 animals. The Group I served as control served with vehicle, Group II animals served as standard which receives diazepam at the dose of 3 mg/kg, through intra-peritoneal route. Group III - XI the animals were treated with the test compounds at the dose of (5 mg/kg, bw, p.o). The test compounds were
administered orally using a tuberculin syringe fitted with oral canula. After 45 minutes of oral administration of the various fractions the animals were placed in to the actophotometer. Movement of the animal is recorded by the light beams present inside the actophotometer for the evaluation of the locomotor activity.

4.2.7. Acute Toxicity Studies

Oral toxicity study for the test compounds were determined as per AOT 423 guidelines. Two out of three animals were died in the group of animals treated with 300 mg/kg, bw, hence the preceding dose was considered as LD50 dose. A dilute quantity of drug i.e., one tenth of the dose (5 mg/kg, bw) was used for further studies.

4.3. Results and Discussion

4.3.1. Anxiolytic activity

Synthesis of aromatic condensed naphthoxazinone derivatives has received considerable attention because of their broad spectrum of biological properties [Olayiwola, G.et al., 2007]. Only compounds such as Quinoxaline diones and their derivatives effect by inducing low index of open arm avoidance in mice in an EPM test model of Anxiolytic activity. Compounds such as Sulphanilamide based quinoxaline and their derivatives show anxiolytic effect in mice that was superior to the effect product by diazepam while the compound such as quinoxaline diones show anxiolytic effect
comparable to diazepam [Obafemi, C. A. et al., 2005]. Some simple 2, 3-quinoxaline diones containing electron donating and electron withdrawing groups and two quinoxalinone only one carbonyl functional group has synthesized and screened for neuropharmalogical activity in mice and rats [Dimmock, J.R.et al., 1994]. Only the Chloro functional group at position 6 and N, N-dibenzylsulphonamido group are essential for neuroproduction against the induced seizers, in addition to the observed good activity of the dibenzylsulfonamido quinoxaline diones. The time spent in the open arms by the animals treated with standard drug diazepam and test compounds was significantly increased when compared to the control group which was treated with the same volume of vehicle. Among the test compounds, all the three substituted quinoxaline series showed significant anxiolytic activity, which shows mild to moderate activity. These compounds show a little difference when compared to the standard drug which indicates that the compounds are equipotent anxiolytic to the standard diazepam. The results are depicted in the figures 36 and 37.

It can be observed from the figure 37 that the time spent in open arm is increased nearer to the standard diazepam. Using the figure 2b, the gradual increase in number of arm entries based on the potency of the individual test compounds, can be witnessed. It should be noted that the increase in open arm entry parameters is the most representative index of anxiolytic activity. Time spent on the central platform appears to be relevant to decision making and
risk assessment, further, the total arm entries is the direct measure reflecting changes in anxiety. The enhanced activity of the quinoxaline drug and its derivatives is expected to be due to the binding site of the ion channel receptor present in the CNS. This in turn, would stimulate the binding of GABA<sub>A</sub> subunit with the GABA receptor, which would produce the prolongation of opening of the channels of Chloride ion. The prolonged opening leads to mild hyper polarization which might be responsible for the noted anxiolytic activity of the test compounds. Quinoxalines act not just by substituting for GABA<sub>A</sub>, which bind at the α-subunit, but also increase the frequency of channel opening events, which leads to an increase in conductance of Chloride ion and also inhibition of the action potential [Brambika, P. et al., 2003].

**Table 14: Antianxiety Activity of Naphthalene based Quinoxalines**

<table>
<thead>
<tr>
<th>S.NO.</th>
<th>GROUP</th>
<th>TIME SPEND IN OPEN ARMS (SEC)</th>
<th>ENTRIES IN OPEN ARM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Control</td>
<td>44.33±6.8</td>
<td>4.33±0.86</td>
</tr>
<tr>
<td>2</td>
<td>STD (Diazepam 0.5mg/kg).</td>
<td>163.33±7.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>13.5±1.25&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>3</td>
<td>Nap-Quin</td>
<td>147.16±9.06&lt;sup&gt;a&lt;/sup&gt;</td>
<td>10.33±0.52&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>Nap-Quin+M</td>
<td>133±5.09&lt;sup&gt;a&lt;/sup&gt;</td>
<td>11.16±1.16&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>Nap-Quin-M</td>
<td>147.66±6.16&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12.33±1.21&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

N=6; Values are expressed as Mean ± SEM; <sup>a</sup>P<0.001, <sup>b</sup>P<0.01 Vs Control group; <sup>c</sup>P<0.001, <sup>d</sup>P<0.01, <sup>e</sup>P<0.05 Vs Standard group; Data were analyzed
by using One way ANOVA followed by Tukey Kramer Multiple comparison Test.

- **Nap Quin** - 2, 3-diphenylbenzo[g]quinoxaline
- **Nap Quin +M** - 2, 3-bis(4-fluorophenyl)benzo[g]quinoxaline
- **Nap Quin- M** - 2,3-bis(4-methylphenyl) benzo[g]quinoxaline

![Graph showing time spent in open arms](image)

**Figure 36.** Anxiolytic activity of naphthalene based quinoxalines in Time spent open arms [STD (Diazepam 0.5 mg/kg)].
N=6; Values are expressed as Mean ± SEM; \(^aP<0.001, ^bP<0.01\) Vs Control group; \(^cP<0.001, ^dP<0.01\) Vs Standard group; Data were analyzed by using One way ANOVA followed by Tukey Kramer Multiple comparison Test.

Figure 37. Anxiolytic activity of naphthalene based quinoxalines in Entries in open arm [STD (Diazepam 0.5 mg/kg)].

[Values are expressed as Mean ± SEM; \(^aP<0.001, ^bP<0.01\) Vs Control group; \(^cP<0.001, ^dP<0.01, ^eP<0.05\) Vs Standard group; Data were analyzed by using One way ANOVA followed by Tukey Kramer Multiple comparison.]
4.3.2. Sedative and Hypnotic activity

Table 15: Sedative and hypnotic activity of Naphthalene based quinoxalines

<table>
<thead>
<tr>
<th>S.NO</th>
<th>GROUP</th>
<th>EXPLORED HOLES DURING 5 MINUTES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Control</td>
<td>15.16±1.16</td>
</tr>
<tr>
<td>2</td>
<td>STD (Diazepam 3mg/kg)</td>
<td>3.1±0.015&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>3</td>
<td>Nap-Quin</td>
<td>2±0.89&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>Nap-Quin+M</td>
<td>2.83±0.98&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>Nap-Quin-M</td>
<td>2.2±0.57&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

- **Nap Quin-** 2, 3-diphenylbenzo[g]quinoxaline
- **Nap Quin+M-** 2, 3-bis(4-fluorophenyl)benzo[g]quinoxaline
- **Nap Ben-** M- 2,3-bis(4-methylphenyl) benzo[g]quinoxaline

Figure 38. Sedative and hypnotic activity of naphthalene based quinoxalines
The hole-board test was used to assess the sedative and hypnotic potential of the test compounds. This test confirmed the CNS calming nature of the test compounds. The results are shown in the figure 38. The number of hole exploration was counted for the period of 5 minutes and the results revealed that the control animal was active whereas the head exploration has been largely reduced in the animals treated with the standard diazepam drug at the dose of 4 mg/kg. The test compounds possess various degrees of whole exploration values. Diazepam is a central nervous system depressant used in the management of sleep disorders such as insomnia; these compounds have a binding site on GABA receptor type-A ionophore complex (GABA$_A$). It decreases activity, moderates excitement, and calms the recipient. GABAergic pathway, since GABAergic transmission can produce profound sedation in mice. The inhibitory action of GABA consists in the opening of chloride channels to allow hyperpolarizing the membrane, leading to CNS depression and resulting in sedative and hypnosis activity. Glutamate and GABA are quantitatively the most important excitatory and inhibitory neurotransmitters, respectively, in the mammalian brain. Thus, receptors for these two neurotransmitters are regarded as important targets for psychotropics drugs. The activity of the test compound may be due to binding with these receptors.
4.3.4. Locomotor activity

Table 16: Locomotor activity of Naphthalene based quinoxalines

<table>
<thead>
<tr>
<th>S.NO</th>
<th>GROUP</th>
<th>MEAN SCORE BEFORE TREATMENT</th>
<th>MEAN SCORE AFTER TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Control</td>
<td>294±6.95</td>
<td>257±15.41</td>
</tr>
<tr>
<td>2</td>
<td>STD (Diazepam 3mg/kg)</td>
<td>277.6±7.78</td>
<td>93.33±7.03&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>3</td>
<td>Nap-Quin</td>
<td>269±19.18</td>
<td>119.83±10.17&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>Nap-Quin+M</td>
<td>257.66±16.84</td>
<td>129.5±10.82&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>Nap-Quin-M</td>
<td>260.66±8.61</td>
<td>105.5±4.34&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

N=6; Values are expressed as Mean ± SEM; <sup>a</sup>P<0.001, <sup>b</sup>P<0.05 Vs Control group; <sup>c</sup>P<0.001Vs Standard group; Data were analyzed by using One way ANOVA followed by Tukey Kramer Multiple comparison Test.

- **Nap Quin-** 2, 3-diphenylbenzo[g]quinoxaline
- **Nap Quin +M-** 2, 3-bis(4-fluorophenyl)benzo[g]quinoxaline
- **Nap Ben- M-** 2,3-bis(4-methylphenyl) benzo[g]quinoxaline
Figure 39. Locomotor activity of naphthalene based quinoxalines

Values are expressed as Mean ± SEM; aP<0.001, bP<0.05 Vs Control group; cP<0.001Vs Standard group; Data were analyzed by using One way ANOVA followed by Tukey Kramer Multiple comparison Test.

The mean score in locomotor activity, before and after the treatment were measured and are shown in the figure 39. There are notable difference observed in the mean score before treatment with standard and the test compounds. After the standard/test drug treatment, the mean score for the diazepam treated group and the test Quinoxaline derivatives treated, together appear lesser active, when compared to the control group. But the test
compounds were observed to show worthier statistics when compared to the standard drug. The results revealed the significant reduction in locomotor activity by the quinoxaline based derivatives. Locomotor activity is believed as an index of alertness and a reduction in that is an indicative of sedative activity. GABA is the major inhibitory neurotransmitter in the CNS and different anxiolytic, muscle relaxant and sedative-hypnotic drugs are expected to exhibit their action via GABA. Therefore, it is possible that the test compounds may act by direct activation of GABA receptors by the test compounds. The increase in efficiency of the natural brain chemical, GABA_A, by the Quinoxaline based derivative is achieved along with the decrease in excitability of neurons.

4.4. Conclusion

The Naphthalene based quinoxalines as a very good option for non-toxic drug possessing anxiolytic, sedative and hypnotic properties. When compared with benzodiazepine drugs, these Naphthalene based quinoxaline drugs shows a little lower effective as an anxiolytic drug and better effect as a sedative and hypnotic.
5. Summary

Synthesis some heterocyclic compounds based on coupling reaction between Pyrimidine derivatives and benzils and as well as Napthalene derivatives and benzils, have been successfully achieved. The effect of para substituent was verified by varying different types of groups and the corresponding results are noted. From the results, the electron withdrawing substituent such as Fluro, yield was better than the electron donating groups such as Methyl. The resulting products were tested for their application in the pharmaceutical drug, using mice as the testing subject. Anxiolytic activity, locomotor activity, Sedative and Hypnotic activity were the few applications tested using the resulting products as the drug.

Pyrimidino-Diazepines were successfully synthesized with greater yield and shorter duration using CTAB as the surfactant. The synthesis in the absence of cationic surfactant resulted in poor yield and time consuming. The solubility of this compound in ethanol, suggests that this product can be used as a challenging drug for the pathogens. These provide a very good option for non-toxic drug possessing better anxiolytic, sedative and hypnotic properties than a few of the reported tricyclic compounds. When compared with Diazepam, this Pyrimidine based drugs shows a little lower effective as an anxiolytic drug and better effect as a sedative and hypnotic. The improvement in locomotor
activity when compared with diazepam shows this drug is better than Diazepam.

Naphthalene based Quinoxalines were successfully synthesized with greater yield (96%) and shorter duration (5 min) using CTAB as the surfactant. The synthesis in the absence of cationic surfactant resulted in poor yield and time consuming (35% and 90 min). The solubility of this compound in ethanol, suggests that this product can be used as a challenging drug for the pathogens. The synthesis of Naphthalene based quinoxaline by this method produced no harmful emissions. These provide a very good option for non-toxic drug possessing anxiolytic, sedative and hypnotic properties.

When compared with benzodiazepine drugs, these Naphthalene based quinoxaline drugs shows a little lower effective as an anxiolytic drug and better effect as a sedative and hypnotic.