

A Mathematical Model for the Effect of TRH Using Fuzzy Reliability Analysis

A. Venkatesh* and S. Elango**

*Assistant Professor, *A. V. V. M. Sri Pushpam College,
Poondi, Thanjavur (Dt), Tamilnadu, India.*

**Assistant Professor, *Anjalai Ammal Mahalingam Engineering College,
Kovilvanni, Tiruvarur (Dt), Tamilnadu, India.*

Abstract

This paper proposes a method for fuzzy reliability estimation where lifetime random variables have a distribution function with fuzzy parameter. The theoretical study for the effect of TRH in GH response in status epilepticus patients was investigated. By using the theory of reliability and α cut set of fuzzy reliability function are calculated by fuzzy gamma, Normal, Weibull and Exponential distribution. The results show that after TRH treatment the GH response was increases in patients. Hence the reliability of TRH treatment is accepted. Also we discussed the suitable fuzzy distribution to find the reliability in the fuzzy environment using fuzzy testing of Hypothesis.

Keywords: Fuzzy reliability function, Thyrotropin Releasing Hormone (TRH), GH,

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1. INTRODUCTION

The reliable engineering is one of the important engineering tasks in design and development of technical system. The conventional reliability of a system is defined as the probability that the system performs its assigned function properly during a

predefined period under the condition that the system behavior can be fully characterized in the context of probability measures. The reliability of a system can be determined on the basis of tests or the acquisition of operational data. The classical reliability theory is based on the probabilistic approach. Essential limitations of this approach are connected with “the problem of the source data” which depends on many factors and which may not correspond to the real conditions of the system’s functioning. Besides, the statistical data used in the probabilistic reliability models fix only the facts of real failures and do not contain the information about the causes of these failures.

In conventional reliability analysis, the failure probabilities of the components of a system are treated as exact values. It is often difficult to obtain data for failure probabilities under changing environmental conditions. Hence fuzzy sets are used to analyze the fuzzy system reliability. It is well known that the conventional reliability analysis, using the probabilities, has been found to be inadequate to handle uncertainty of failure data and modeling. To overcome this problem, the concept of fuzzy approach has been used in the evaluation of the reliability of a system. Fuzzy set theory was first introduced by Zadeh [1] in 1965. Singer [2] presented a fuzzy set approach for fault tree and reliability analysis. Cai et al. [3, 4] gave a different insight by introducing the possibility assumption and fuzzy state assumption to replace the probability and binary state assumptions. The theory of fuzzy reliability was proposed and developed by several authors, Cai [3], Wen and Zhang [5]

The tripeptide thyrotropin-releasing hormone (TRH) is known to control the synthesis and secretion of pituitary thyrotropin (thyroid stimulating hormone, TSH) and prolactin [7]. TRH-secreting neurons are located in the medial portions of the paraventricular nuclei (PVN) of the hypothalamus; their axons terminate in the medial portion of the external layer of the median eminence [8]. TRH is originally discovered in the hypothalamus, consistent with its classical role as a hypothalamic hypophysiotrophic factor, the effects of TRH on the immune system can be either stimulatory or inhibitory and are state dependent. TRH is now known to be distributed extensively in extra hypothalamic brain structures [9,13] and in other organs and tissues [10]. Similarly, receptors for TRH are found throughout the central and peripheral nervous system as well as in other organs and tissues [11]. The widespread distribution of TRH and its receptors suggests other important functions for this tripeptide, including possible critical interactions with other biological systems [12, 13].

Testing statistical hypotheses is one of the most important areas of statistical analysis. In many situations, the researchers in the field of data analysis are interested in testing a hypothesis about the population parameter. In traditional testing, the observations of sample are crisp and a statistical test leads to the binary decision. However, in real life, the data sometimes cannot be recorded precisely. The statistical hypothesis

testing under fuzzy environments has been studied by many authors. In traditional statistics all parameters of the mathematical model and possible observations should be well defined. Sometimes such assumption appears too rigid for the real-life problems, especially while dealing with linguistic data or imprecise requirements. To relax this rigidity fuzzy methods are incorporated into statistics.

2. FUZZY RELIABILITY FUNCTION

Assume that X and U are two crisp sets. Let failure rate function be fuzzy and represented by a fuzzy set $\bar{H}(t), \bar{H}(t) = \{h, \mu_{\bar{H}(t)}, h \in X\}$. The α - cut fuzzy set of $\bar{H}(t)$ is $\bar{H}_\alpha(t) = \{h \in X / \mu_{\bar{H}(t)} \geq \alpha\}$. Note that $\bar{H}_\alpha(t)$ is a crisp set. Suppose that $\bar{H}(t)$ is a fuzzy number. Then for each choice of α - cut, we have an interval $\bar{H}_\alpha(t) = \{h_1(t), h_2(t)\}$. By the convexity of the fuzzy number, the bounds of the interval are function of α and can be obtained as $\bar{h}_{1\alpha} = \min \mu_{\bar{H}(t)}(\alpha)$ and $\bar{h}_{2\alpha} = \max \mu_{\bar{H}(t)}(\alpha)$ respectively.

Let $\phi: X \rightarrow U$ be a bounded continuous differentiable function from X to U . We wish to calculate the fuzzy set (fuzzy reliability functions) induced on U by applying ϕ for the set $\bar{H}(t)$. If we write $u = \phi(h)$, where $h \in X$ and $\bar{R}(t) = \{u, \mu_{\bar{R}(t)}(u) / u = \phi(h), u \in U\}$ then the membership function of $\bar{R}(t)$ is defined by the extension principle $\mu_{\bar{R}(t)}(u) = \sup_{h \in X} \{\mu_{\bar{H}(t)}(h) / u = \phi(h)\}$.

We know that if $\bar{H}(t)$ is normal and convex and ϕ is bounded, then $\bar{R}(t)$ is also normal and convex. Therefore we can calculate the corresponding interval $[r_1(t), r_2(t)] = \phi(\bar{H}_\alpha(t))$ Where $r_1(t)$ and $r_2(t)$ correspond, respectively, to the global minimum and maximum of ϕ over the space $\bar{H}_\alpha(t)$ at the α level.

$$r_1(t) = \min \phi(h), \text{ such that } h_1(t) \leq h \leq h_2(t)$$

$$r_2(t) = \max \phi(h), \text{ such that } h_1(t) \leq h \leq h_2(t)$$

The crisp reliability function of an object is $R(t) = P(T \geq t) = 1 - F(t)$. Now we define the fuzzy reliability by means of the fuzzy distribution function $\bar{R}(t) = \bar{P}(\bar{T} > t) = 1 - \bar{F}(t) \forall t \in [0, \infty)$. Where \bar{T} is a fuzzy random variable which describes the vagueness of the time “t” and the uncertainty of the probability distribution whose distribution functions is $\bar{F}(x) = \bar{P}(X < x)$ and X is the random variable.

3. MATERIALS AND METHODS

The reliability function for gamma distribution is defined by

$$\begin{aligned} R(t) &= \frac{1}{\Gamma(r)} \int_t^{\infty} \lambda^r u^{r-1} e^{-\lambda u} du \\ &= \frac{1}{\Gamma(r)} \Gamma(r, \lambda t) \end{aligned}$$

The α - cut of fuzzy reliability function for gamma distribution is

$$\bar{R}(t)[\alpha] = [R_1(\alpha), R_2(\alpha)]$$

$$\text{Where } R_1[\alpha] = \text{Max} \frac{1}{\Gamma(r)} \Gamma(r, \lambda t) / \lambda \in \bar{\lambda}[\alpha], r \in \bar{r}[\alpha]$$

$$R_2[\alpha] = \text{Min} \frac{1}{\Gamma(r)} \Gamma(r, \lambda t) / \lambda \in \bar{\lambda}[\alpha], r \in \bar{r}[\alpha]$$

The reliability function for Normal distribution is defined by $R(t) = 1 - \varphi\left\{\frac{t-\mu}{\sigma}\right\}$

The α - cut of fuzzy reliability function for Normal distribution is

$$\bar{R}(t)[\alpha] = [R_1(\alpha), R_2(\alpha)]$$

$$\text{Where } R_1[\alpha] = \text{Max} \left\{ 1 - \varphi\left\{\frac{t-\mu_1[\alpha]}{\sigma_1[\alpha]}\right\} \right\}$$

$$R_2[\alpha] = \text{Min} \left\{ 1 - \varphi\left\{\frac{t-\mu_2[\alpha]}{\sigma_2[\alpha]}\right\} \right\}$$

The reliability function for weibull distribution is defined by

$$R(t) = e^{-\left(\frac{t}{\theta}\right)^\beta}$$

The α - cut of fuzzy reliability function for weibull distribution is

$$\bar{R}(t)[\alpha] = [R_1(\alpha), R_2(\alpha)]$$

$$\text{Where } R_1[\alpha] = \text{Max} \left\{ e^{-\left(\frac{t}{\theta}\right)^\beta}, \theta \in \bar{\theta}[\alpha], \beta \in \bar{\beta}[\alpha] \right\}$$

$$R_2[\alpha] = \text{Min} \left\{ e^{-\left(\frac{t}{\theta}\right)^\beta}, \theta \in \bar{\theta}[\alpha], \beta \in \bar{\beta}[\alpha] \right\}$$

The reliability function for Exponential distribution is defined by

$$R(t) = e^{-\lambda t}$$

The α - cut of fuzzy reliability function for Exponential distribution is

$$\bar{R}(t)[\alpha] = [R_1(\alpha), R_2(\alpha)]$$

Where $R_1[\alpha] = \text{Max} \{e^{-\lambda t}, \lambda \in \bar{\lambda}[\alpha]\}$

$$R_2[\alpha] = \text{Min} \{e^{-\lambda t}, \lambda \in \bar{\lambda}[\alpha]\}$$

4. Application:

Let us take a experiment conducted by [14] in the status epilepticus patients, the serum GH levels before and after injection of TRH during status epilepticus are shown in Table. 3.1. GH levels before TRH injection ranged between 0.4 and 8.8mU/l, with a median of 1.5mU/l and a mean of 2.7mU/l. In all six status patients, GH levels increased at least two fold within 15–30 min after the TRH injection. In one patient (no. 4) the value at 45 min was the highest for that patient, but it was also the last, due to missing blood samples. GH levels had fallen in the other five patients by 60 min after the TRH injection. The peak concentrations of GH after injection ranged from 1.9 to 19.4mU/l; median levels were 6.5mU/l and the mean was 8.4mU/l.

Table: 4.1 GH response to TRH during treatment in 6 patients status epilepticus

Time(min)	0	20	40	60	80	100	120	140	160	180
Serum Prolactin (µg/ml)	8	18	10	8	7	6	5	4	3	2

RESULTS AND DISCUSSION

The scale parameter and shape parameter of gamma distribution are respectively

$$\lambda = 0.342 \text{ and } r = 2.427.$$

Let the corresponding Triangular fuzzy numbers are

$$\bar{\lambda} = [0.395, 0.342, 0.350]$$

$$\bar{r} = [2.420, 2.427, 2.435]$$

And the corresponding α cuts are

$$\bar{\lambda}[\alpha] = [0.395 + 0.053\alpha, 0.350 - 0.008\alpha]$$

$$\bar{r}[\alpha] = [2.420 + 0.007\alpha, 2.435 - 0.008\alpha]$$

The scale parameter and shape parameter of Normal distribution are $\mu = 7.10$ and $\sigma = 2.13$

$$\bar{\mu} = [6.99, 7.10, 7.50]$$

$$\bar{\mu}[\alpha] = [6.99 + 0.11\alpha, 7.50 - 0.40\alpha]$$

$$\bar{\sigma} = [2.0, 2.13, 2.50]$$

$$\bar{\sigma}[\alpha] = [2.0 + 0.13\alpha, 2.50 - 0.37\alpha]$$

The scale parameter and shape parameter of weibull distribution are $\theta = 8.029$ and $\beta = 1.80$

$$\bar{\theta} = [8.00, 8.029, 8.05]$$

$$\bar{\beta} = [1.78, 1.80, 1.84]$$

$$\bar{\theta}[\alpha] = [8.00 + 0.029\alpha, 8.05 - 0.021\alpha]$$

$$\bar{\beta}[\alpha] = [1.78 + 0.02\alpha, 1.84 - 0.02\alpha]$$

The scale parameter Exponential distribution is $\lambda = 0.141$ and here

$$\bar{\lambda} = [0.139, 0.141, 0.145], \quad \bar{\lambda}[\alpha] = [0.139 + 0.002\alpha, 0.145 - 0.004\alpha]$$

Table. 4.2 Fuzzy and crisp reliability function for Gamma Distribution

Time (in Hrs.)	$R_1[\alpha]$	$R_2[\alpha]$	$\mathbf{R(t)}$
0	1	1	1
0.05	0.993296791	0.990639946	0.99128461
0.1	0.964645688	0.950684535	0.953766592
0.15	0.908443	0.873455379	0.880689158
0.2	0.824785738	0.761878339	0.774159132
0.25	0.718521495	0.626608931	0.643562776
0.3	0.598165393	0.483067579	0.503060909
0.35	0.47414504	0.347245728	0.367879441
0.4	0.356682693	0.231638962	0.25051492
0.45	0.253875533	0.142765862	0.158179485
0.5	0.170493263	0.080965574	0.092241837

Table.4.3 Fuzzy and crisp reliability function for Normal Distribution

Time (in Hrs.)	$R_1[\alpha]$	$R_2[\alpha]$	R(t)
0	0.999555961	0.998227261	0.999275925
0.05	0.999515569	0.998118017	0.999217209
0.1	0.999471833	0.99800284	0.999154197
0.15	0.999424508	0.997881462	0.999086616
0.2	0.999373335	0.997753607	0.999014179
0.25	0.999318037	0.997618987	0.998936583
0.3	0.999258324	0.997477309	0.998853511
0.35	0.999193886	0.997328271	0.998764631
0.4	0.999124397	0.997171558	0.998669594
0.45	0.999049513	0.997006851	0.998568035
0.5	0.998968868	0.996833819	1

Table.4.4 Fuzzy and crisp reliability function for Weibull Distribution

Time (in Hrs.)	$R_1[\alpha]$	$R_2[\alpha]$	R(t)
0	1	1	<i>I</i>
0.05	0.9998807	0.99991302	0.999892914
0.1	0.999590352	0.999688636	0.999627155
0.15	0.999157133	0.999343551	0.999226597
0.2	0.998593863	0.998885734	0.998702279
0.25	0.997908882	0.998320499	0.998061436
0.3	0.997108342	0.997651837	0.99730944
0.35	0.996197109	0.996882955	0.996450559
0.4	0.995179216	0.996016549	0.995488346
0.45	0.99405811	0.995054951	0.99442585
0.5	0.998048781	0.998658894	0.993265755

Table.4.5 Fuzzy and crisp reliability function for Exponential Distribution

Time (in Hrs.)	$R_1[\alpha]$	$R_2[\alpha]$	R(t)
0	1	1	1
0.05	0.993074095	0.992776218	0.992974793
0.1	0.986196159	0.985604619	0.985998939
0.15	0.979365858	0.978484826	0.979072093
0.2	0.972582864	0.971416464	0.972193909
0.25	0.965846848	0.964399164	0.965364045
0.3	0.959157485	0.957432554	0.958582163
0.35	0.952514451	0.95051627	0.951847925
0.4	0.945917427	0.943649947	0.945160996
0.45	0.939366093	0.936833226	0.938521044
0.5	0.932860133	0.930065747	0.93192774

From Table 4.2 we observe that when time increases the lower and upper reliability values are decreases. And the Difference between the crisp reliability and lower reliability is greater than the difference of crisp and upper reliability values. From this we note that the crisp reliability is very nearer to the Fuzzy upper Values when using fuzzy Gamma Distribution.

From Table 4.3 we observe that when time increases the lower and upper reliability values are decreases. And the Difference between the crisp reliability and lower reliability is less than the difference of crisp and upper reliability values. From this we note that the crisp reliability is very nearer to the Fuzzy lower Values when using fuzzy Normal Distribution.

From Table 4.4 we observe that when time increases the lower and upper reliability values are decreases. And the Difference between the crisp reliability and lower reliability is nearer to difference of crisp and upper reliability values. From this we note that the crisp reliability is very nearer to the Fuzzy lower and upper values by fuzzy Weibull distribution

From Table 4.5 we observe that when time increases the lower and upper reliability values are decreases. And the Difference between the crisp reliability and lower reliability is nearer to the difference of crisp and upper reliability values. From this we note that the crisp reliability nearer to the Fuzzy lower and upper values by fuzzy Exponential Distribution.

4.1. TESTING OF HYPOTHESIS

Testing statistical hypotheses is one of the most important areas of statistical analysis. In many situations, the researchers in the field of data analysis are interested in testing a hypothesis about the population parameter. In traditional testing, the observation of sample is crisp and a statistical test leads to the binary decision. However, in real life, the data sometimes cannot be recorded precisely. The statistical hypothesis testing under fuzzy environments has been studied by many authors. In traditional statistics all parameters of the mathematical model and possible observations should be well defined. Sometimes such assumptions appears too rigid for the real-life problems, especially while dealing with linguistic data or imprecise requirements. To relax this rigidity fuzzy methods are incorporated into statistics using the values in Table 3.2, 3.3,3.4,3.5, we set the Null hypothesis as follows,

For Gamma distribution and Normal distribution

Let $H_0: \bar{d} = 0$ there is no significant difference between the two methods

$H_1: \bar{d} > 0$ (One tailed test)

The test statistic is $\bar{t}_L = \frac{\bar{d}_L}{\frac{s_L}{\sqrt{n}}}$ where $\bar{d}_L = \bar{G}_L - \bar{N}_L$ and $S^2 = \frac{\sum(d_L - \bar{d}_L)^2}{n-1}$, $s = \sqrt{S^2}$

The test statistic is $\bar{t}_U = \frac{\bar{d}_U}{\frac{s_U}{\sqrt{n}}}$ where $\bar{d}_U = \bar{G}_U - \bar{N}_U$ and $S^2 = \frac{\sum(d_U - \bar{d}_U)^2}{n-1}$, $s = \sqrt{S^2}$

For Gamma distribution and Weibull distribution

Let $H_0: \bar{d} = 0$ there is no significant difference between the two methods

$H_1: \bar{d} > 0$ (One tailed test)

The test statistic is $\bar{t}_L = \frac{\bar{d}_L}{\frac{s_L}{\sqrt{n}}}$ where $\bar{d}_L = \bar{G}_L - \bar{W}_L$

The test statistic is $\bar{t}_U = \frac{\bar{d}_U}{\frac{s_U}{\sqrt{n}}}$ where $\bar{d}_U = \bar{G}_U - \bar{W}_U$

For Gamma distribution and Exponential distribution

Let $H_0: \bar{d} = 0$ there is no significant difference between the two methods

$H_1: \bar{d} > 0$ (One tailed test)

The test statistic is $\bar{t}_L = \frac{\bar{d}_L}{\frac{s_L}{\sqrt{n}}}$ where $\bar{d}_L = \bar{G}_L - \bar{E}_L$

The test statistic is $\bar{t}_U = \frac{\bar{d}_U}{\frac{s_U}{\sqrt{n}}}$ where $\bar{d}_U = \bar{G}_U - \bar{E}_U$

For Normal distribution and Weibull distribution

Let $H_0: \bar{d} = 0$ there is no significant difference between the two methods

$H_1: \bar{d} > 0$ (One tailed test)

The test statistic is $\bar{t}_L = \frac{\bar{d}_L}{\frac{s_L}{\sqrt{n}}}$ where $\bar{d}_L = \bar{N}_L - \bar{W}_L$

The test statistic is $\bar{t}_U = \frac{\bar{d}_U}{\frac{s_U}{\sqrt{n}}}$ where $\bar{d}_U = \bar{N}_U - \bar{W}_U$

For Normal distribution and exponential distribution

Let $H_0: \bar{d} = 0$ there is no significant difference between the two methods

$H_1: \bar{d} > 0$ (One tailed test)

The test statistic is $\bar{t}_L = \frac{\bar{d}_L}{\frac{s_L}{\sqrt{n}}}$ where $\bar{d}_L = \bar{N}_L - \bar{E}_L$

The test statistic is $\bar{t}_U = \frac{\bar{d}_U}{\frac{s_U}{\sqrt{n}}}$ where $\bar{d}_U = \bar{N}_U - \bar{E}_U$

For Weibull distribution and Exponential distribution

Let $H_0: \bar{d} = 0$ there is no significant difference between the two methods

$H_1: \bar{d} > 0$ (One tailed test)

The test statistic is $\bar{t}_L = \frac{\bar{d}_L}{\frac{s_L}{\sqrt{n}}}$ where $\bar{d}_L = \bar{W}_L - \bar{E}_L$

The test statistic is $\bar{t}_U = \frac{\bar{d}_U}{\frac{s_U}{\sqrt{n}}}$ where $\bar{d}_U = \bar{W}_U - \bar{E}_U$

Using the values in Table 4.2, 4.3, 4.4, 4.5 we set the Null hypothesis as follows and the test values are given in the table 4.6

Table.4.6: Fuzzy and crisp reliability function for Weibull Distribution

S.No.	Distribution 1	Distribution 2	\bar{t}	D.O.F	Tabulated t	H_0	H_1
1	Gamma Lower	Normal Lower	3.657	10	2.228	Rejected	Gamma distribution better than Normal distribution
	Gamma Upper	Normal upper	3.864	10	2.228	Rejected	
2	Gamma Lower	Weibull Lower	3.661	10	2.228	Rejected	Gamma distribution better than Weibull distribution
	Gamma Upper	Weibull upper	3.881	10	2.228	Rejected	
3	Gamma Lower	Exponential Lower	3.548	10	2.228	Rejected	Gamma distribution better than Exponential distribution
	Gamma Upper	Exponential upper	3.795	10	2.228	Rejected	
4	Normal lower	Weibull lower	2.987	10	2.228	Rejected	Normal distribution better than Weibull distribution
	Normal upper	Weibull upper	2.713	10	2.228	Rejected	
5	Normal lower	Weibull Lower	4.991	10	2.228	Rejected	Normal distribution better than Weibull distribution
	Normal upper	Weibull upper	4.804	10	2.228	Rejected	
6	Weibull Lower	Exponential Lower	5.184	10	2.228	Rejected	Weibull distribution better than Exponential distribution
	Weibull upper	Exponential upper	5.163	10	2.228	Rejected	

5. CONCLUSION

In this paper the level of GH after the administration of TRH in the Status epilepticus Patients using fuzzy reliability analysis by various distributions was studied. From the above study, it was observed that after TRH treatment the releasing level of GH is increased and we showed that the fuzzy reliability values after TRH treatment is increased in the lower α cuts and they are decreased in the upper α cuts in fuzzy

Gamma, Exponential and Normal distribution. But in the Weibull Distribution the reliability values is decreased in the lower α cuts and they are increased in the upper α cuts. From the test statistic result we can say the Fuzzy gamma distribution is better than the other distributions to find the reliability in fuzzy environment.

REFERENCES

- [1]. Zadeh, L. A.. Fuzzy sets. *Information Control*; 8: 338-353, 1965
- [2]. Singer, D. A fuzzy set approach to fault tree and reliability analysis. *Fuzzy Sets and Systems*, 34, 2: 145-55, 1990.
- [3]. Cai, K.Y., Wen, C.Y., and Zhang, M.L. Fuzzy variables as a basis for a theory of fuzzy reliability in the possibility context. *Fuzzy Sets and Systems*, 42, 2:145-172. 1991.
- [4]. Cai, K.Y., Wen, C.Y., and Zhang, M.L... Posbist reliability behavior of typical systems with two types of failures. *Fuzzy Sets and Systems*, 43, 1:17-32, 1991.
- [5]. Cai, K.Y., Wen, C.Y., and Zhang, M.L... Fuzzy states as a basis for a theory of fuzzy reliability. *Microelectronic Reliability*,33, 1: 2253-2263, 1993.
- [6]. Gau, W.L. and Buehrer, D.J. Vague sets. *IEEE.Tran.* 1993.
- [7]. Nillni, E. A., & Sevarino, K. A. The biology of pro-thyrotropin-releasing hormone derived peptides. *Endocr Rev* 20(5), 599–648, (1999).
- [8]. Guillemin, R. Peptides in the brain the new endocrinology of the neuron. *Science* 202, 390–402. (1978).
- [9]. Winokur, A., & Utiger, R. D. Thyrotropin-releasing hormone: regional distribution in rat brain. *Science* 185, 265–266, (1974).
- [10]. Lechan, R. M. Update on thyrotropin-releasing hormone. *Thyroid Today* 16,1–11. (1993).
- [11]. Sun, Y., Lu, X., & Gershengorn, M. C. Thyrotropin-releasing hormone receptors similarities and differences. *J Mol Endocrinol* 30(2), 87–97, (2003).
- [12]. Gary, K. A., Sevarino, K. A., Yarbrough, G. G., Prange, A. J., Jr., & Winokur, A. Thethyrotropin-releasing hormone (TRH) hypothesis of homeostatic regulation implications for TRH-based therapeutics. *J Pharmacol Exp Ther.* 305(2), 410–416. (2003).
- [13]. Yarbrough, G. G., Kamath, J., Winokur, A., & Prange, A. J., Jr Thyrotropin-releasing hormone (TRH) in the neuroaxis: therapeutic effects reflect physiological functions and molecular actions. *Med Hypotheses* 69(6),

1249–1256, (2007).

- [14]. Ulla Lindbom, Anna-Lena Hulting, and Torbjorn Tomson “Paradoxical GH response to TRH during status epilepticus in man”, *European journal of Endocrinology*, 140, 307-314,(1999)



