

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Life Sciences

Research Article.....!!!

Received: 16-10-2014; Revised: 21-10-2014; Accepted: 01-11-2014

STUDY OF FC RECEPTOR-LIKE PROTEIN3 AND ITS BINDING EFFICIENCY WITH HERBAL AND ALLOPATHIC ANTIBIOTICS

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Keywords:

FCRL3, Active sites,
Docking, Herbal drug,
Allopathic drug

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ABSTRACT

This study is aimed to determine the effect of drug (herbal and allopathic) on the FCRL3. FCRL3 protein sequence was collected from Uni-prot, The composition of amino acids was determined by using Protparam. The tertiary structure of FcRL 3 was predicted by using CPH modeling server and visualized through Rasmol. Ramachandran plot was performed for FCRL3 using Rampage software. The active sites were predicted by CASTp. The docking of FCRL3 with selected herbal (Acetaminophen) and allopathic (methimazole) was performed by Hex 6.3.

INTRODUCTION

Bioinformatics is the field of science in which biology, computer science and information technology merge to form a single discipline. Bioinformatics has not only become essential for basic genomic and molecular biology research, but is having a major impact on many areas of biotechnology and biomedical sciences.

GRAVES DISEASE

Graves disease, named after Robert Graves circa (1830) is an autoimmune disease characterized by hyperthyroidism due to circulating autoantibodies [Yeung *et.al.*, 2013]. Thyroid-stimulating immunoglobulins (TSIs) bind to and activate thyrotropin receptors, causing the thyroid gland to grow and the thyroid follicles to increase synthesis of thyroid hormone. Graves disease is associated with pernicious anemia, vitiligo, diabetes mellitus type 1, autoimmune adrenal insufficiency, systemic sclerosis, myasthenia gravis, Sjogren syndrome, rheumatoid arthritis and systemic lupus erythematosus [Brix *et.al.*, 2001]. Graves disease, along with Hashimoto thyroiditis, is classified as an autoimmune thyroid disorder [Homsanit *et.al.*, 2001]. Symptoms of the resultant hyperthyroidism are mainly insomnia, hand tremor, hyperactivity, hair loss, excessive sweating, shaking hands, itching, heat intolerance, weight loss despite increased appetite, diarrhea, frequent defecation, palpitations, muscle weakness and skin warmth and moistness [Brent, 2008]. Further signs that may be seen on physical examination are most commonly a diffusely enlarged (usually symmetric), nontender thyroid, lid lag, excessive lacrimation due to Graves ophthalmopathy, arrhythmias of the heart, such as sinus tachycardia, atrial fibrillation and premature ventricular contractions and hypertension [Elizabeth *et.al.*, 2008]. People with hyperthyroidism may experience: psychosis, mania, anxiety, agitation and depression [Bunevicius and Prange, 2006]. Thyroid stimulating immune globulins recognize and bind to the thyrotropin receptor (TSH receptor). It mimics the TSH to that receptor and activates the secretion of thyroxine (T4) and triiodothyronine (T3) and the actual TSH level will decrease in the blood plasma. Early reports, not widely circulated, of cases of goitre with exophthalmos were published by the Italians Giuseppe Flajina and Antonio Giuseppe Testa, in 1802 and 1810, respectively. This case was not published until 1825, but still 10 years ahead of Graves [Ljunggren, 1983]. The incidence of Graves Disease in Olmstead County, Maryland (USA) was found to be 30 cases per 100,000 population annually. A thorough examination of an English town by Tunbridge and associates found an incidence of 100–200 cases per 100,000 per year, significantly higher than the previous estimates. In this report, it was also found that 2.7% of women and 0.23% of men had Graves disease or a history of it.

This survey also noted that goiter was present in 15% of women, anti thyroid antibodies in 10.3% of women and that hypothyroidism was about two-thirds as common as Graves disease. A recent update in this area showed a continuing incidence of 80 cases/100,000 women/year. Data attest to a lifelong incidence of autoimmune thyroid disease of $> 6\%$, comprised roughly equally by Graves disease, Hashimoto's thyroiditis and idiopathic hypothyroidism. It is a protein that in humans is encoded by the FCRL3 gene [Davis *et.al.*, 2001]. This gene encodes a member of the immunoglobulin receptor superfamily and is one of several Fc receptor-like glycoproteins clustered on the long arm of chromosome 1. [Davis *et.al.*, 2002]. Unlike the classical Fc receptors, there is no strong evidence that suggests that FCRLs bind to the Fc portion of antibodies [Santiago *et.al.*, 2010].

HERBAL DRUG

Acetaminophen medication are available over the counter that able to reduce swelling (inflammation) and pain. Anti-inflammatory products are effective in reducing joint and muscular pain and the associated swelling with Graves disease They are also excellent choices for arthritic pain and swelling.

ALLOPATHIC DRUG

Methimazole ATD (anti thyroid drug) is used to help lower thyroid hormone levels in all causes of hyperthyroidism with the exception of thyroiditis. One recent Medline Update recommends ATD as the primary treatment for Graves disease. Common anti-thyroid drugs or ATDs include propylthiouracil or PTU, methimazole and carbimazole. Carbimazole, which is primarily used outside of the United States, is essentially the same as methimazole.

MATERIAL AND METHODS

The structures of FCRL3 were predicted with the help of bioinformatics tools and also docking with selected antibiotics such as herbal drug use of Drug bank (Acetaminophen) and allopathic drug use of (Methimazole) were analyzed (Table 1, Fig.2). Human FCRL3 Protein sequence was retrieved from the UNI-PROT protein sequence data base. By the use of CFSSP the secondary structure was determined. The tertiary structure of FCRL3 was predicted by using CPH 3.2 server and visualized using rasmol. The Ramachandran plot was performed for FCRL3 by using Rampage software. CASTp predicted the active sites.

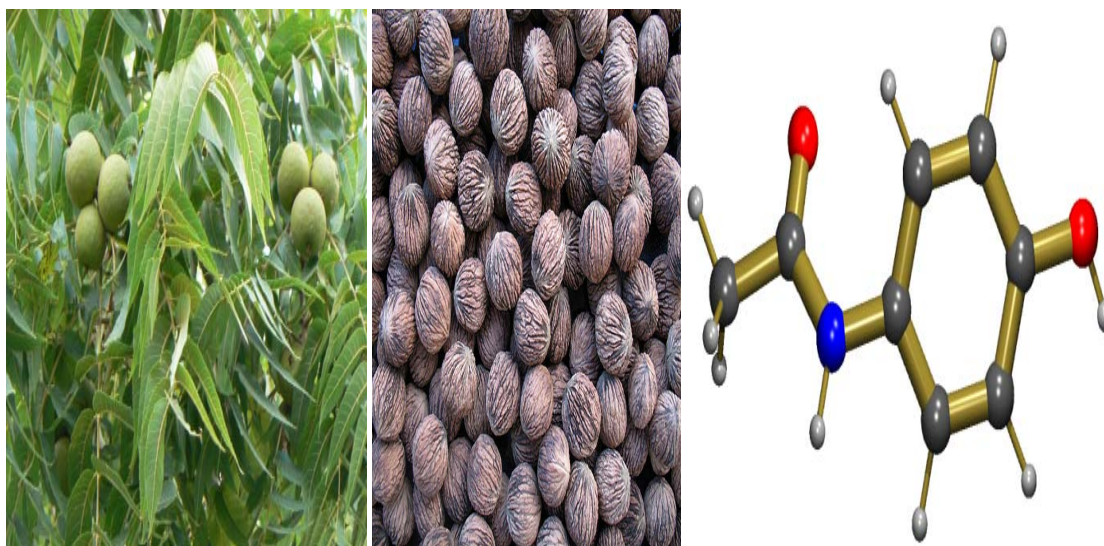
RESULTS

Human FCRL3 sequence was retrieved from the UNI-PORT protein sequence data base. The structures of FCRL3 was predicated with the help of Bioinformatics tools and also docking with selected antibiotic such as herbal drug (Acetaminophen) and allopathic drug (Methimazole) was

analyzed. (Table 1, Fig. 2). Amino acid composition was determined for the human FCRL3. FCRL3 has 734 amino acids with the molecular weight of 80856.1. It's theoretical PI is 6.56. The aliphatic amino acids serine is present in highest number (82). Further the amino acids Alanine, Glutamic, Glycine, Lucien, Serine, Threonine and Valine are also higher in number as 45, 45, 29 and 28 respectively. The negatively charged amino acid aspartic is lesser than the glutamic acid. The positively charged amino acid arginine is lesser than the Serine. It has the estimated half-life of 30hours. Its instability index is 46.16 and its aliphatic index is 85.40. It has the grand average of hydropath city. FCRL3 has 11295 atoms. Among them the carbon, hydrogen, nitrogen, oxygen and sulphur atoms are present in 3556, 5603, 1019, 1095 and 22 numbers respectively. The secondary structure of FCRL3 has 402 % alpha helix, 103 % extended strand, 34.8 % beta turns and 38. 1% random coil.

The Ramachandran plot showed that FCRL3 has 225amino acids (87.5%) are in favoured region 23 (8.9%) are allowed region and 9 (3.4%) are in outlier region. This proves that the predicated model is acceptable. CASTp predicated the actives sites. FCRL3 structure has 38 active sites. FCRL3 has four large active sites (35, 36, 37, and 38) and one small active site (9). Docking of FCRL3 with selected one herbal antibiotic (Acetaminophen) and one allopathic antibiotic (Methimazole) were performed by the use of the tool Hex 6.3.

Fig :1- Herbal drug: Acetaminophen-Chemical Structure



Allopathic drug: Methimazole-Chemical Structure

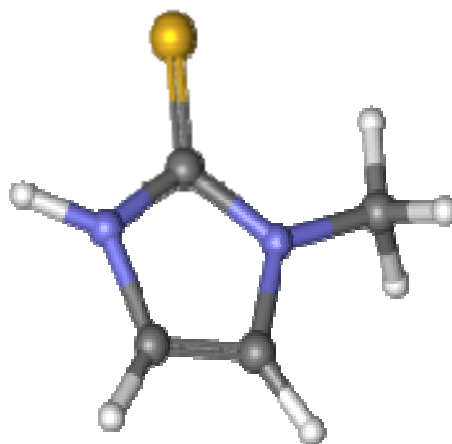
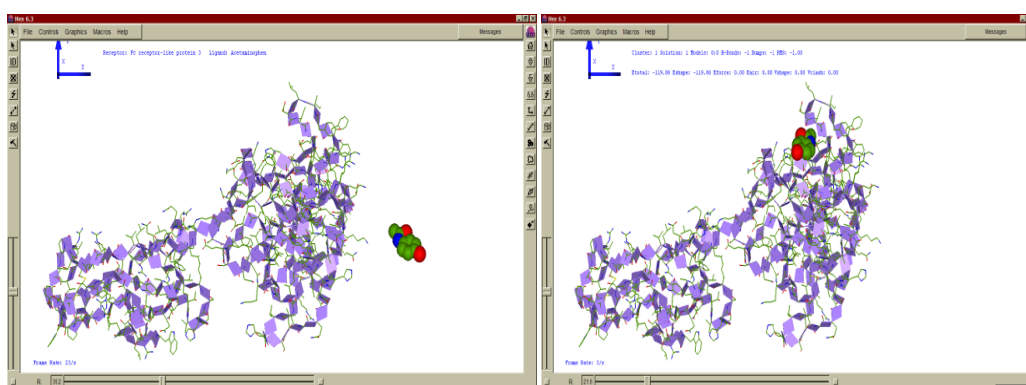


Fig: 2 - Herbal drug docking Graves disease FCRL3 with Acetaminophen

a) Before Docking

b) After Docking



Allopathic drug docking: Graves disease fcrl3 with Methimazole

a) Before Docking

b) After Docking

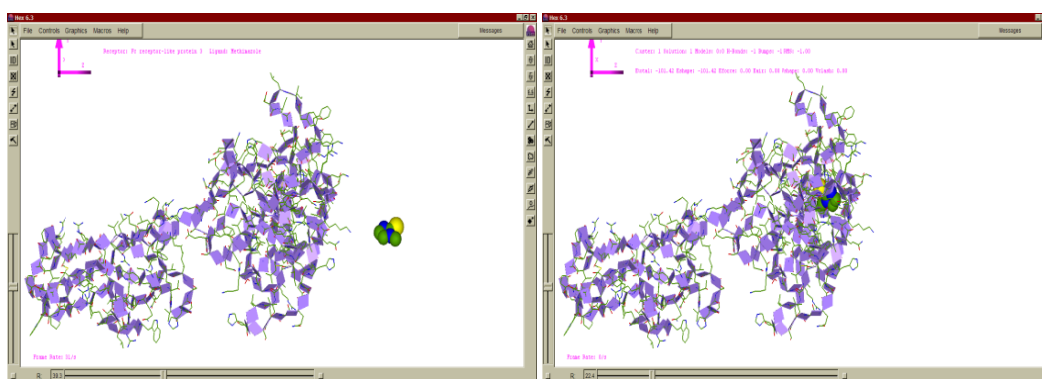


Table-1: Herbal drug and Allopathic drug docking in Graves disease FCRL3

HERBAL DRUG					
LIGAND	E.TOTAL	E.SHAPE	E.FORCE	BUMPS	RMS
Acetaminophen	-119.86	-119.86	0.00	-1	-1.00
ALLOPATHIC DRUG					
LIGAND	E.TOTAL	E.SHAPE	E.FORCE	BUMPS	RMS
Methimazole	-101.42	-101.42	-0.00	-1	-1.00

DISCUSSION

Docking of FCRL3 protein with selected one herbal antibiotic (Acetaminophen) and one allopathic antibiotic (Methimazole) were performed by the use of the tool Hex 6.3. Graves disease antibiotics Acetaminophen and Methimazole have showed higher binding efficiency, ie-119.86 and ie-101.42 respectively with FCRL3 protein when compared with the herbal and allopathic antibiotics (Table 1).

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