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Application of Bioinformatics Tools in Validation of an *In-vivo* Research on Plant Extracts

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Abstract

Introduction: In the current trend of information technology, where numerous applications and brands are developing each day in different sectors, immense expansion in the area with huge potential has led to a boom in this sector.[1] Its application in the field of biological research as bioinformatics has led to the development of various research databases, softwares and weblinks. This has created a new vision in the minds of biologists and scientists to approach in an improved manner to fill the gaps between discovered and undiscovered. The use of bioinformatics based applications has also helped the researchers in identifying the validity of a research.

Objective: The present study involves the use of bioinformatics database and tools to validate the results of an *in-vivo* research on natural plant extracts like estradiol, alkaloids etc. The extracts consist of functional groups that make them suitable to bind to specific proteins in the human body.

Methodology: The protein sequences were retrieved using a database called National Centre for Biotechnology Information (NCBI). This database has a specific tool- FASTA which can retrieve protein sequences present in the nature. The binding of plant extracts to this sequence was analyzed using STITCH database. Results- It was found that the extract estradiol could bind to the identified protein sequence. This result was obtained within fraction of seconds.

Conclusion: The application of tools in bioinformatics has not only decreased the manmade errors but also reduced the time in result validation and analysis.

Keywords: Bioinformatics, Databases, FASTA, STITCH, NCBI

1. Introduction

The advancement in information technology has not only created opportunities for the youth but has also played an important role in developing economy worldwide Information technology has widened its applications in all the sectors including biological sciences and health care [1]. Its application in the field of biological research as bioinformatics has led to the development of various research databases, softwares and weblinks. The databases like National Centre for Biotechnology Information (NCBI), EnTREZ, FASTA, BLAST etc. consist of largest nucleotides and protein collection databases of the worldwide Nucleotide sequence Database Collaboration [2].

FASTA is a Fast Alignment Sequence Test for Application that is mainly used to generate protein sequences existing in the nature [3]. Another database called STITCH (Search tool for interacting chemicals) is a platform to identify anticipated interactions among chemical compounds and proteins [4]. These applications have also helped the researchers in identifying the validity of a research in biological and related sciences. In one of the studies, the FASTA format of the proteins retrieved from NCBI database were used as an input to run the algorithm [5].

In this study, various bioinformatics database and tools have been used to validate the results of an *in-vivo* research. The research is based on binding of natural plant extract- estradiol on female reproductive hormones- luteinizing hormone and follicle stimulating hormone.

2. Methodology

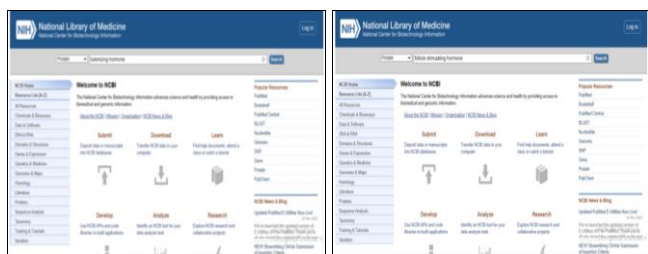### 2.1 Retrieval of Hormonal Sequences

Hormones are chemicals that are synthesized by glands in the body to control and regulate the cellular activity. These are proteinaceous in nature. The protein sequences for luteinizing and follicle stimulating hormone were retrieved using a database called National Centre for Biotechnology Information (NCBI). This database has a specific tool- Fast Alignment Sequence Test for Application (FASTA) which can retrieve protein sequences present in the nature.

2.1.1 For Luteinizing Hormone

The homepage of NCBI was opened from the website (https://www.ncbi.nlm.nih.gov/) [6]. In "all databases" tab, selected "protein" and inserted the term "luteinizing hormone" in the search bar and then pressed "search" button (Figure 1a). A new web page appeared, chosen link "leuteinizing hormone beta subunit, partial [Homo sapiens] 56 aa protein". When clicked on the link, the available information regarding the hormone and FASTA link appeared. Then, clicked on "FASTA". The sequence available for the desired hormone was obtained.

2.1.2 For Follicle Stimulating Hormone

The homepage of NCBI was opened from the site (https://www.ncbi.nlm.nih.gov/) [6]. In "all databases" tab, selected "protein" and inserted the term "follicle stimulating hormone" in the search bar and then pressed "search" button (Figure 1b). A new web page appeared, chosen link "follicle stimulating hormone [Homo sapiens] 129 aa protein". When clicked on the link, the available information regarding the hormone and FASTA link appeared. Then, clicked on "FASTA". The sequence available for the desired hormone was obtained.

(a) Luteinizing hormone   (b) Follicle-stimulating hormone

Fig 1: NCBI Homepage

2.2 Binding of Plant Extracts with Hormonal Sequences

To check the binding of natural plant extracts with retrieved hormonal sequences, a database called STITCH (Fig 2) was used.

2.2.1 Luteinizing Hormone sequence

The homepage of STITCH database was opened from the site (http://stitch.embl.de/) [7]. On the left side of the page, selected the term "protein sequences". Below the "SEARCH" (on right side) pasted the retrieved luteinizing hormone protein sequence. Then, from the list below the term "Organism", "Homo sapiens" was selected to insert. When clicked on the "Search" button, another page opened that showed the list of available proteins related to the sequence. From them, selected the stitch protein- LHB. Then, pressed the "continue" button on top right corner of the page. The network of protein bound to different chemical structures was obtained.

2.2.2 Follicle Stimulating Hormone Sequence

The homepage of STITCH database was opened from the site (http://stitch.embl.de/) [7]. On the left side of the page, selected the term "protein sequences". Below the "SEARCH" (on right side) pasted the retrieved follicle stimulating hormone protein sequence. Then, from the list below the term "Organism", "Homo sapiens" was selected to insert. When clicked on the "Search" button, another page opened that showed the list of available proteins related to the sequence. From them, selected the stitch protein- FSHB. Then, pressed the "continue" button on top right corner of the page. The network of protein bound to different chemical structures was obtained.
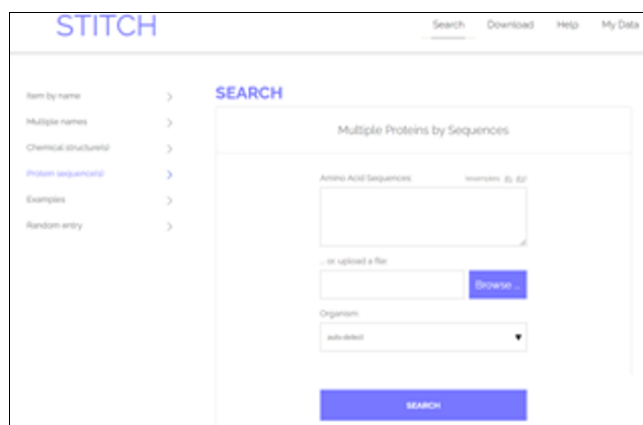
Fig 2: STITCH Database

3. Results and Discussion

3.1 Hormonal Sequence

While retrieving the sequence from FASTA, it provides an accession number for each retrieved item. Accession number is a unique identifier that is assigned to achieved materials within the database. The accession number for identified sequence of luteinizing hormone obtained was >QPB74003.1, while for follicle stimulating hormone was >AAA52476.1. The FASTA protein sequences retrieved for luteinizing and follicle stimulating hormone are mentioned in the Table 1 and Figure 3 (a,b). Further, the binding of plant extracts to this sequence was analyzed using STITCH database.

In a study FASTA was used to retrieve sequence of a mutated gene TP53-binding protein 1 having protein sequence as VADPVDSSNLDTCGSISEVIEQLPQPNR [4].

Table 1: Hormone Sequences Retrieved Using FASTA

| Hormone	Accession No.	FASTA Protein sequence
Luteinizing hormone	>QPB74003.1	>QPB74003.1 luteinizing hormone beta subunit, partial [Homo sapiens] GLLLLLLLLSMGGTWASKEPLRPRCRPINATLAVEKEGCPVCITVNTTICAGYCPTM
Follicle stimulating hormone	>AAA52476.1	>AAA52476.1 follicle-stimulating hormone [Homo sapiens] MKTLQFFFLFCCWKAICCNSCELTNITIAIEKEECRFCISINTTWCAGYCYTRDLVYKDPARPKIQKTCT FKELVYETVRVPGCAHHADSLYTYPVATQCHCGKCDSDSTDCTVRGLGPSYCSFGEMKE

(a) Luteinizing hormone

(b) Follicle stimulating hormone

Fig 3: Retrieved Hormonal Sequence using FASTA

3.2 Analysis of Plant Extracts Binding to Hormonal Sequences using STITCH database

Luteinizing Hormone and Follicle stimulating hormone- The binding of natural plant extract with luteinizing hormone and follicle stimulating hormone was analyzed using STITCH database. As shown in the Fig 4, it was found that estradiol group of the plant extract could bind to testosterone hormone that is indirectly bounded to the LHB (Luteinizing hormone β-polypeptide). The interaction score obtained through the analysis was 0.659. This can lead to activation in secretion of luteinizing hormone in the human body.

For FSHR (Follicle stimulating hormone), the estradiol group can directly bind to the FSH which may result in increased activity of the hormone. The interaction score obtained through the analysis was 0.820.

According to Kuhn *et al*. 2014, through a STITCH database the number of high confidence protein-chemical interactions in humans increased by 45% [8].

Source: http://stitch.embl.de/cgi/network.pl?taskId=VnBWs9GAfZlt
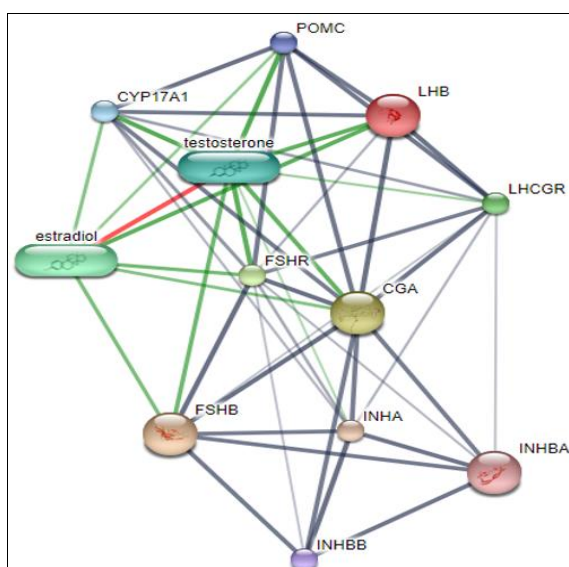
Fig 4: Hormone- Estradiol Interactions using STITCH database

4. Conclusion

A research is not only collection of results and data but it also requires interpretation and validation of that data which makes a research complete and important [9]. In biological research and health care it is said to be a time-taking process. With the advancement of information technology, the recent tools and softwares in bioinformatics has overcome this scenario of awaiting results in biological and related fields. Not only this, but validation of an *in-vivo* research is also possible now. In this study, it was found that the natural plant extract estradiol could bind to the identified hormonal sequence within the human body. It is one of the important findings of this research. Also, this result was obtained within fraction of seconds. The application of tools in bioinformatics has not only decreased the manmade errors but also reduced the time in result validation and analysis.

5. References

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