Internet Based Drug Design of New Opioid Analgesics

Avnish Kaur, Meenakshi Mehra*

Himachal Institute of Pharmacy, Paonta Sahib, Distt- Sirmour, Himachal Pradesh, India

***Correspondence:** Meenakshi Mehra, Himachal Institute of Pharmacy, Paonta Sahib, Distt- Sirmour, Himachal Pradesh, India. **E-Mail:**mehrameenakshi1991@gmail.com

Abstract

The development of new drug with its therapeutic potential is one of the most vital process in pharmaceutical industry. Now a day, there is development & importance of computational chemistry including molecular docking & a SAR study which deals with pharmacophore based drug design approach. Also, the methodology linked with modification of the target based drug discovery has been performed by using various computational tools. Thus, the present study deals with the Structural Activity Relationship study & pharmacophore based drug design approaches with the use of internet based tools which are free of cost & compatible with any platform. Here, attempts are made to design OPIORPHIN analogue by pharmacophore study to design more potent or equivalent opioid analgesic using free internet based tools by using Java platform to input structure, calculate its drug likeness, molecular properties & toxicity which are important parameters for structure based rational drug design.

Keywords: Computational chemistry, computational tools, molecular docking, Opioid Analgesics, Opiorphin, pharmacophore, Structural Activity Relationship.

Introduction

In today's world, the biggest scientific challenges is to design a potent opioid analgesic. For that, structure based drug designing has become increasingly much in use to design potent drug like molecules but the main problem of this Structure based drug design is the use of high price computational software because these high price softwares are not easily available to individuals, also they are incompatible with many modern operating systems such as WINDOWS 7 64-bit, ANDROID OS, Chromium OS etc. Also many modern processors such as i5, i7 etc. have some compatibility issues with this modern computational drug design software. For the same reasons INTERNET based drug designing has become a popular tool for design of new potent drug like molecules as they are independent of operating system & processors. INTERNET based drug design on the basis of SAR & pharmacophore study becomes a fruitful tool for modern structure based rational drug design. This INTERNET based tools are easy to handle because it uses JAVA platform to input structure & calculate the drug likeness & molecular properties.. Opiorphin has been taken as a prototype to design new drug like molecules. Opiorphin is an endogenous chemical compound first isolated from human saliva. This compound has a painkilling effect greater than that of morphine. It works by stopping the normal breakup of enkephalins, natural pain-killing opioidsin the spinal cord. It is a relatively simple molecule consisting of a five-amino acid polypeptide, Gln-Arg-Phe-Ser-Arg.. INTERNET based drug design tools have been used to analysise the structural analogues of opiorphin for their drug like behavior[1-10].

Materials & Methods

Opiorphin has the following molecular structure:

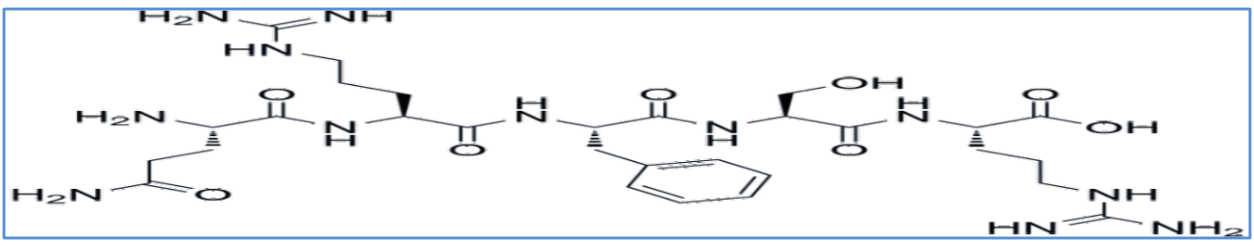


Fig 1: Opiorphin molecular structure

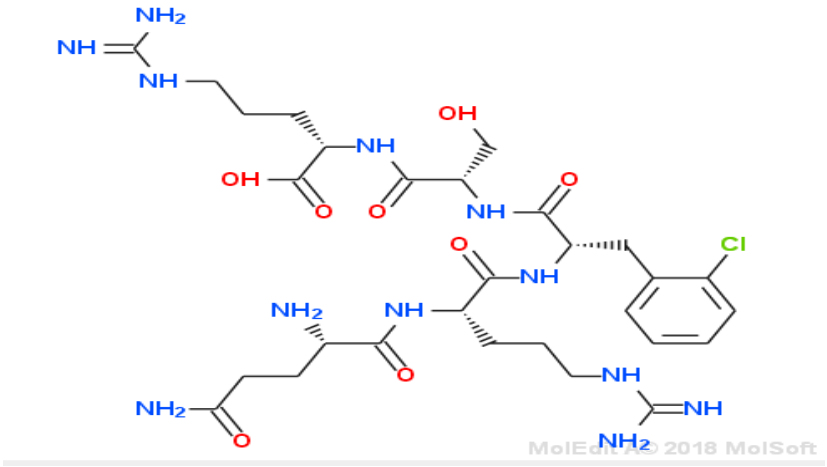
The new designed drug like molecules has been designed by taking Opiorphin as prototype & substituting the atoms on the benzene ring of the Opiorphin structure[11-15].

In case of Opiorphin, various substitutions are done like 1 Cl or 1 CH_3 atom is added to the benzene ring or anaphylene ring, 4 Cl atoms are added to the benzene ring or anaphylene ring. By using SAR & pharmacophore study, substitutions are done to get high degree likeness score than that of prototype Opiorphin. The structural analogues based drug design has been performed using MOLSOFT molecules in drug likeness & molecular property prediction tool. The new designed molecules on the basis of SAR & pharmacophore study have been inputted in JME molecular editor & different properties have been calculated. The lazar toxicity of all these designed drugs have been performed using internet based lazar toxicity prediction tool. These works have been performed by using WINDOWS 7 64-bit operating system having Intel core 2 duo processor.

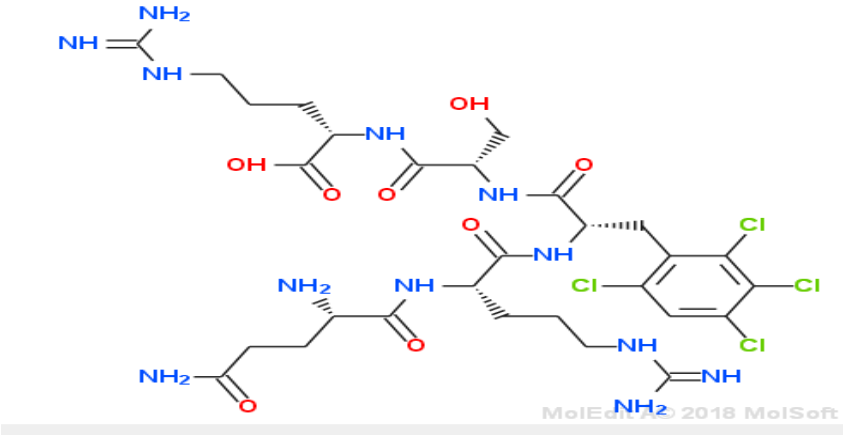
Result & Discussion

Drug likeness score of Opiorphin analogues

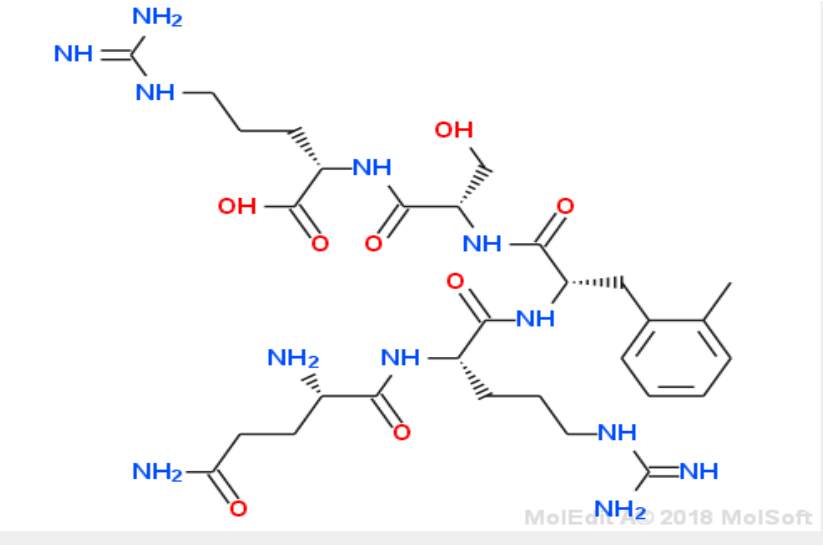
New drug like Opiorphin analogues have been listed below. Drug likeness score is predicted by MOLSOFT. By SAR & pharmacophore study, substitutions are done in such a way that the drug likeness score of new drug like molecules are near that of prototype.



Molsoft drug likeness score: -0.43; molecule ID: Opiorphin 1



Molsoft drug likeness score: 0.09; molecule ID: Opiorphin 2



Molsoft drug likeness score: -0.68; molecule ID: Opiorphin 3

Table 1: **Drug likeness score**

Molecule ID	**Mol Log P**	**Molecular Weight**	**Drug Likeness**
Opiorphin	-6.11	692.37	-0.84
Opiorphin 1	-5.51	726.33	-0.43
Opiorphin 2	-3.73	828.22	0.09
Opiorphin 3	-5.86	596.34	-0.68

The above data shows that different analogues of Opiorphin increases the drug likeness score when calculated by MOLSOFT[16].

Lazar toxicity of all these molecules have been predicted using in silico lazar toxicity prediction tool. From lazar toxicity prediction study, it is evident that the entire new designed drug like molecules are found to be non-carcinogenic in rodents & rats[17].

Table 2:**Predicted lazar toxicity**

Molecule ID	**Carcinogenic in rodent**	**Carcinogenic in mouse**	**Carcinogenic in rat**
Opiorphin	Non-carcinogenic	Non-carcinogenic	Non-carcinogenic
Opiorphin 1	Non-carcinogenic	Non-carcinogenic	Non-carcinogenic
Opiorphin 2	Non-carcinogenic	Carcinogenic	Non-carcinogenic
Opiorphin 3	Non-carcinogenic	Non-carcinogenic	Non-carcinogenic

Table 3: Predicted Mutagenecity & Penetration

Molecule ID	Blood Brain Barrier Penetration (Human)	Mutagenecity
Opiorphin	Non-penetrating	Non-mutagenic
Opiorphin 1	Non-penetrating	Non-mutagenic
Opiorphin 2	Non-penetrating	Non-mutagenic
Opiorphin 3	Non-penetrating	Non-mutagenic

A foresaid molecule designed & the way is new & hoping that current tool may be useful for developing new era for bringing into force new opioid analgesic drug with affordable cost. All the above designed & developed drug like molecules are designed on the basis of SAR studies & pharmacophore study. All the molecules have equipotent effect & are found to be equivalent active opioid analgesic as compared to the prototype Opiorphin. Also the predicted molecules found to have non-carcinogenic, non-mutagenic in nature with low level of toxicity. The internet based tool here used is found to be easy to use & compatible. The molecule designed above & the method is novel.

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