ISSN: 2320 - 4230

Journal of Drug Discovery and Therapeutics 1 (5) 2013, 47-54

REVIEW ARTICLE

CORRELATION BETWEEN CHEMINFORMATICS AND BIOINFORMATICS IN DRUG DISCOVERY: A FARSIGHT OF PHARMACY-THE MILLENNIUM OATH

***Vikramkumar Vishnubhai Patel[1], Prof. (Dr.) Dhrubo Jyoti Sen[2], Prof. Satyanand Tyagi[3]**

[1]Research Associate, Veeda Clinical Research®, Shivalik Plaza-A, Near IIM, Ambawadi, Ahmedabad, Gujarat, India-380015

[2]Department of Pharmaceutical Chemistry, Shri Sarvajanik Pharmacy College, Gujarat Technological University, Arvind Baug, Mehsana, Gujarat, India-384001

[3]President & Founder, Tyagi Pharmacy Association (TPA) & Scientific Writer (Pharmacy), New Delhi, India-110074

ABSTRACT

All drugs are chemicals but all chemicals are not drugs*….This statement always focuses towards the footsteps of a new drug discovery by information technology which is concerned with the drug designing which is followed by two info systems: Cheminformatics is the application of software technology to the chemical science in all about its reflection towards the chemistry of a molecule and Bioinformatics is the application of the same software technology in the organizing the biocompatible drug molecules to the macromolecules.*

Pharmacy is a subject that is running on it's two feet: chemistry and biology. The footsteps of the both are lying side by side. Lack of one of these two subjects the balance will be disrupted. Chemistry of a drug molecule is superimposed by the biological activity of the same. Recent technology is flourishing day by day according to the progress of basic pharmaceutical science to combat with diseases caused by microorganisms and anomalies in the normal feedback system in living beings. Advanced technology is spreading rapidly to manufacture the new molecules, which could be helpful for diagnosis, treatment and cure of diseases to accept the challenge for making milestone for the new millennium. It is a playground for a chemist and a biologist to play a game with the newer technology.

KEYWORDS: Bioinformatics, Cheminformatics, Drug, Receptor, QSAR, Nanotechnology, Docking, HTS, *in-silico*

INTRODUCTION:

The Drug is a chemical substance either obtained from synthetic or natural source having definite 3D-chemical network, having capacity to fit on the 3D-bioreceptor platform or has controlling capacity to inhibit the malfunction of biochemical and physicochemical behavior *in-vivo*. According to these phenomena, the particular substance to be a drug should follow all these points.[1-4]

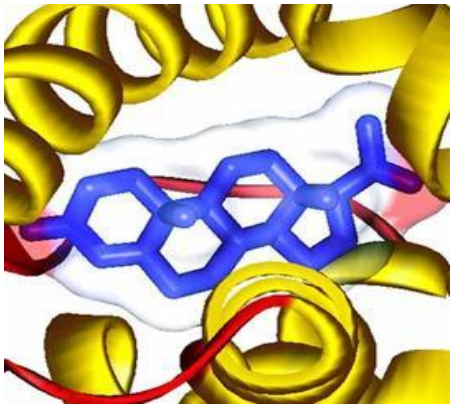


Figure 1: Drug and Receptor

A specific drug entity either inorganic or organic moiety has a definite crystal structure having compact matrix design, having polarity, having specific bond length, having bond energy, having hydrophobicity/hydrophilicity to occupy the site on the macromolecular bed of receptor to show its biological response. Every drug has some active functional group to which the derivatization is possible for making it as repository form for prolongation of its biological response. The entire structural network is also helpful to design the drug polymer matrix due to the formation of polymer pockets to load the drug molecules.[5-8]

***Corresponding author:** Vikramkumar Vishnubhai Patel | **Email:** vikram311287@gmail.com

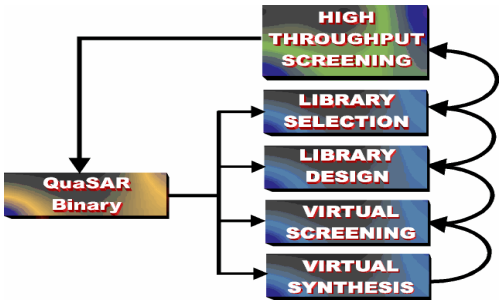


Figure-2: Design of Drug Process

The Medicine is a formulated device of drug in which active pharmaceutical ingredient (API) is embedded with excipients to form various dosage forms marketed in wholesale or retail shops after dispatch from pharmaceutical company.

Figure 3: Medicine in Formulation

Pharmaceutical globalization is a hot topic in the recent edition of technology transfer. Pharmacy and science meet at the interface to form pharmaceutical science, which is scattered in various directions according to the need of modern healthcare system.

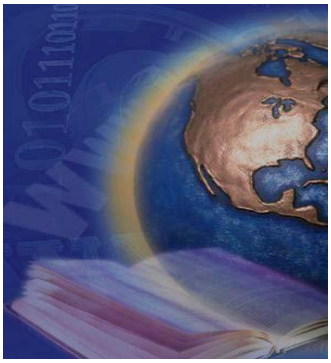


Figure 4: Technology Transfer

Transfer of newer technology from the pages of book to the global corners and the implementation of newer concept of molecular design in the interface of science and technology of pharmaceutical science reflects on drug discovery.[9-11]

Figure 5: Pharmaceutical Globalization

Numerous kinds of technology in pharmacy are being implemented in the umbrella of bioscience for necessary medication to the patient compliances. The basic pharmacy originates from the grass root of level of natural products known as Veshaja, which was an excellent tool to cure the patients from various diseases. The active constituents present in the flora and fauna are the gold coin to climb on a ladder of great hope for coming future. In the modern market of pharmaceuticals, most of the drugs, which are being incorporated, are designed according to the mother component present in the natural source.[12-14]

Figure 6: Natural Drugs

Design of new drug molecule is motivated and highlighted from the structural variation, molecular tailoring of the mother component. Alkaloids, steroids, glycosides, tannins, carbohydrates, flavones, amino acids, iridoids, etc are found in plenty in holistic medicines. Structural design of new molecules is possible according to the active mass of the main constituents through molecular modeling, and rational drug design and finally by QSAR studies. Newer concepts like nanotechnology and combinatorial science either (chemistry or biology) is vividly used now a day in the newer horizon of pharmaceutical science.[15-17]

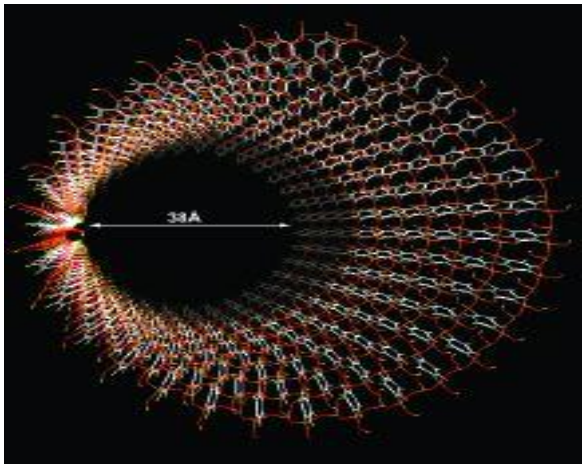


Figure 7: Nanotechnology

Nanotechnology is an amalgamation of science and technology that has affected the measurement in the lowest units (nanometer-billionth of a meter). Dendrimers, Nanowires, Carbon Nanotubes, Quantum Dots are now used in the field of nanotechnology giving high efficiency and profitability. Nanotechnology is a valuable contribution of the profound research by scientists and engineers to create new systems with novel functionalities. Supramolecular chemistry is also being implemented in polymer science to ensure the novel drug delivery system in transdermal delivery as well as in nano world to make a solid matrix of integration of so many nanoparticles to form a fullerene structure. Calixarenes, Rotaxanes, Liposome technology all are used to make a solid matrix of polymer to hold the nanotubes loaded with drug particles to make a sustained release or controlled release formulation by using the latest technology to get the better response.[18,19]

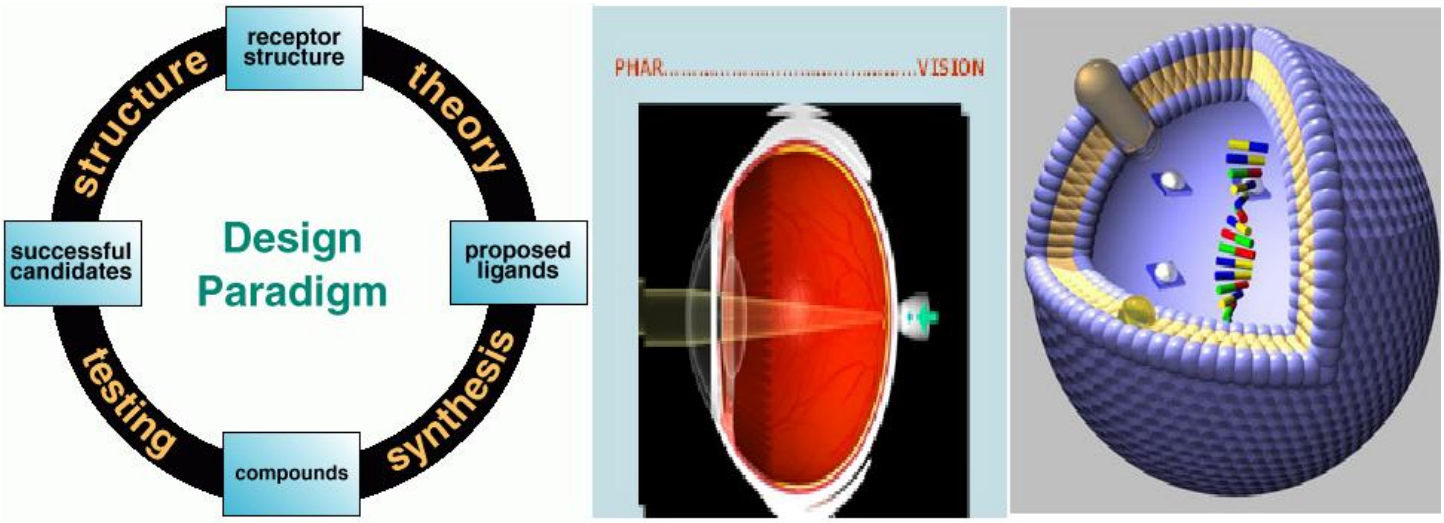


Figure 8: Far sight of pharmacy in latest technology

CHEMINFORMATICS INCLUDE:
Chemical Informatics
Chemo-Informatics & Chemi-Informatics
Chemo metrics
Data Mining
Data Designing
Structure Activity Relationship

BIOINFORMATICS INCLUDE:
Scientific Computing
Genome Sequence
Structure Prediction
Protein Sequence
Molecular Simulation

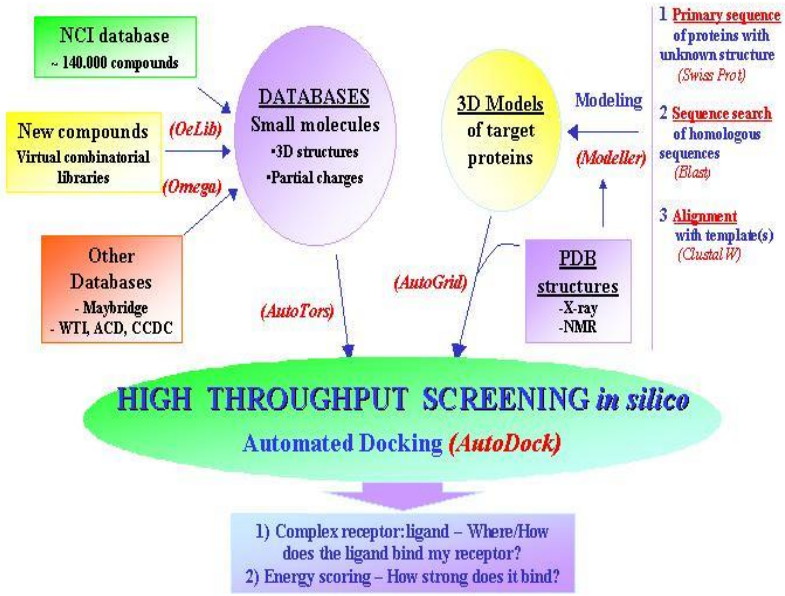


Figure 9: HTS by AutoDock

Indian pharmaceutical and biotech majors like DR REDDY'S LABORATORIES, WOCKHARDT, SUN PHARMA, NICHOLAS PIRAMAL AND RANBAXY are now deploying a cheminformatics for lead screening of promising drug molecules of greater importance at earlier stages, as well as for the optimization of new chemical entities (NCE).[20]

Till now, cheminformatics and bioinformatics combine used by ORCHID, RANBAXY, ALEMBIC, GLEN MARK, WOCKHARDT AND SUN PHARMA.

One of the major application of this relation is drug-receptor binding site or (target discovery). Here in the example it is illustrated that exact molecule of the drug bind (fit) at the bioreceptor site and shows activity.[21]

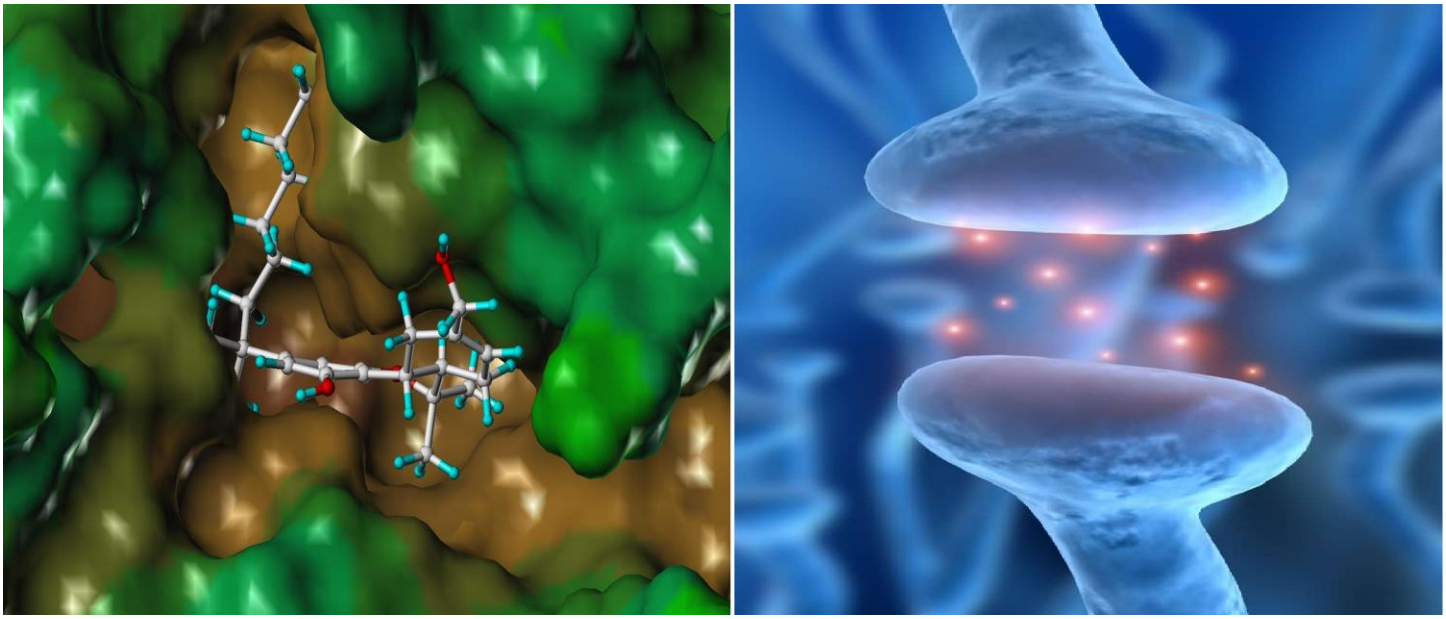


Figure 10: Receptor binding site for the drug

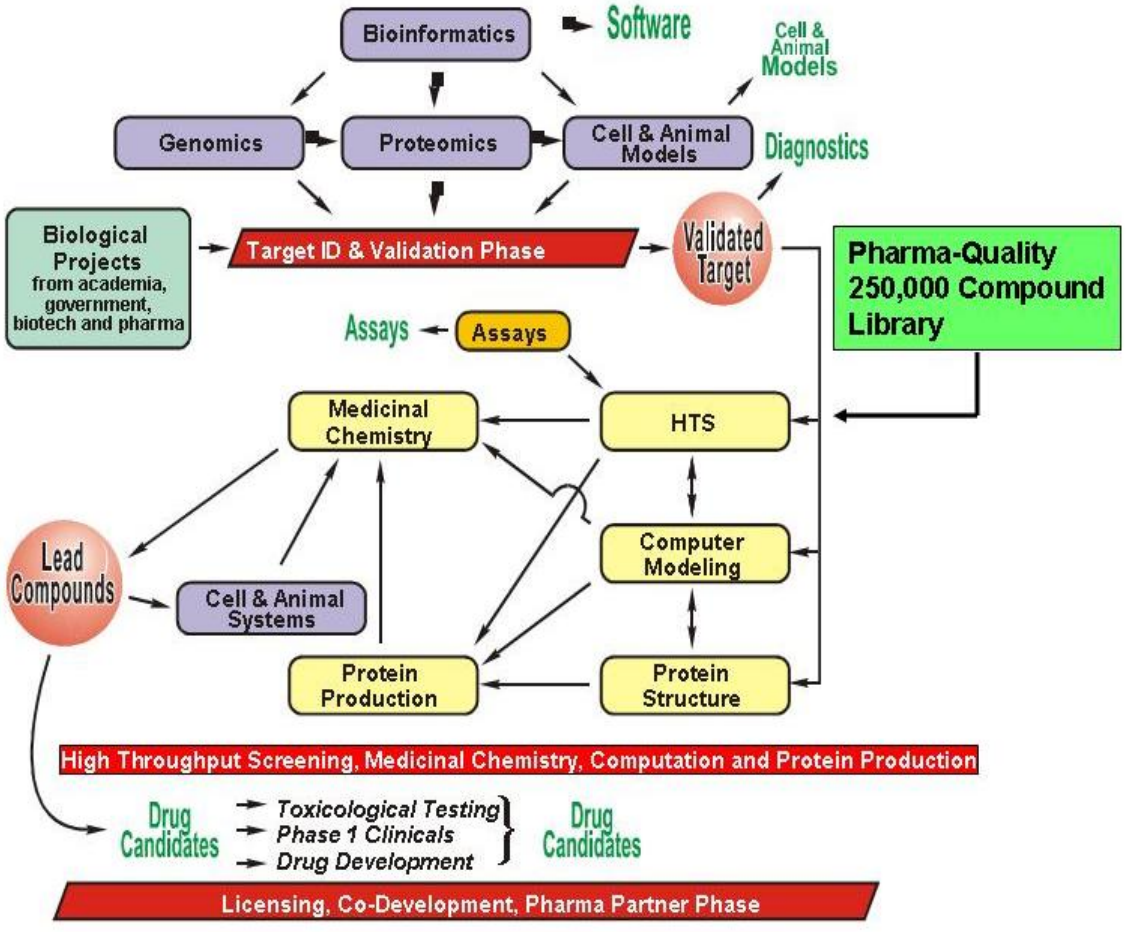
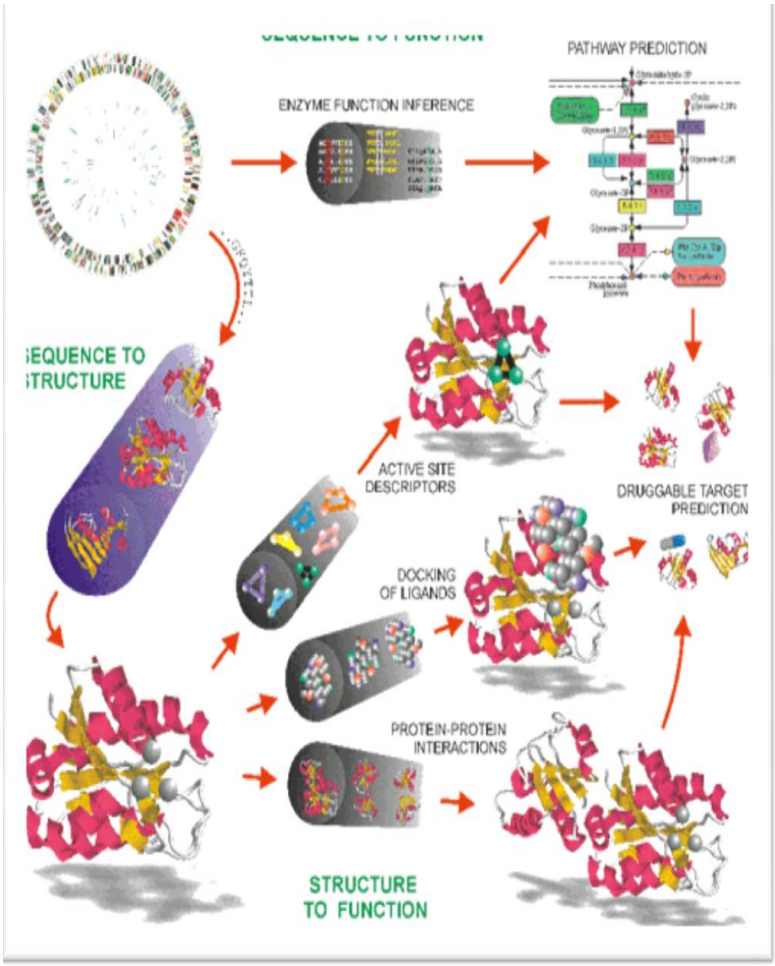
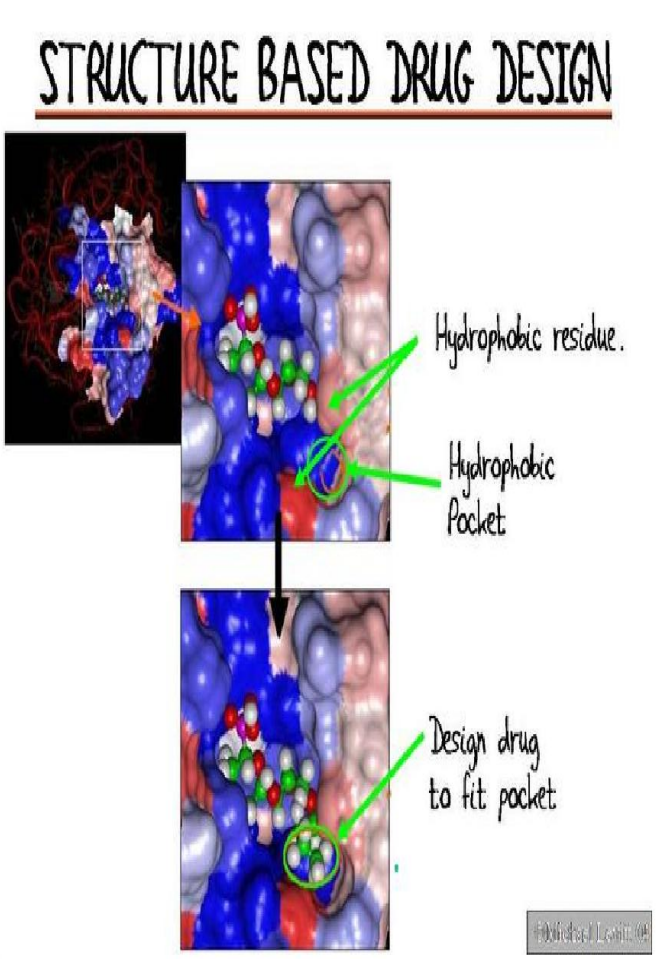
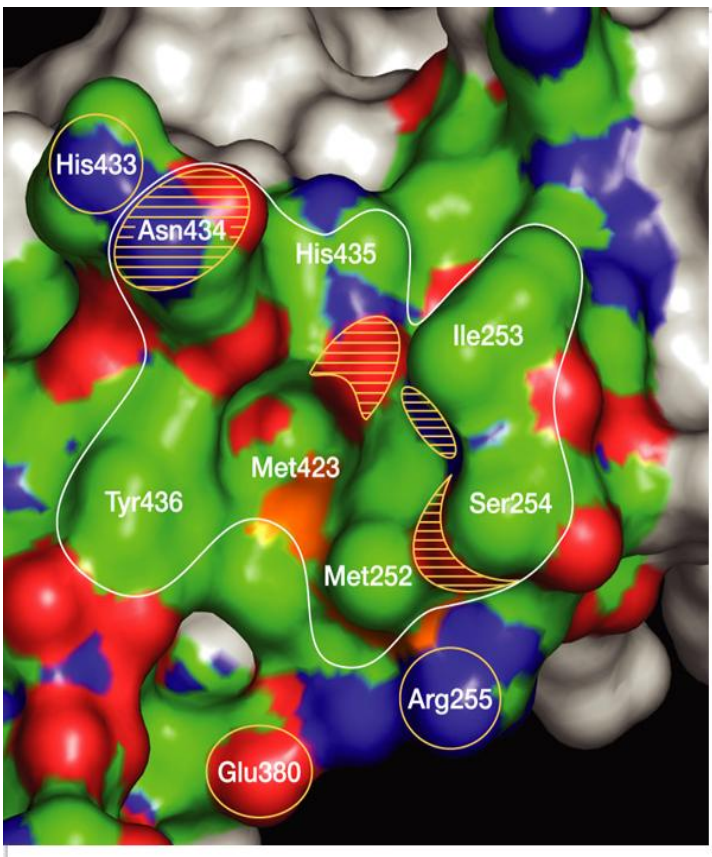


Figure 11: Bioinformatics flowchart

Protein-protein interactions can be quantitatively analyzed for structural variations resulted from site-directed mutagenesis can be studied by bioinformatics and the exact molecule for the repair of that deformation can be studied by the use of cheminformatics.[22,23]







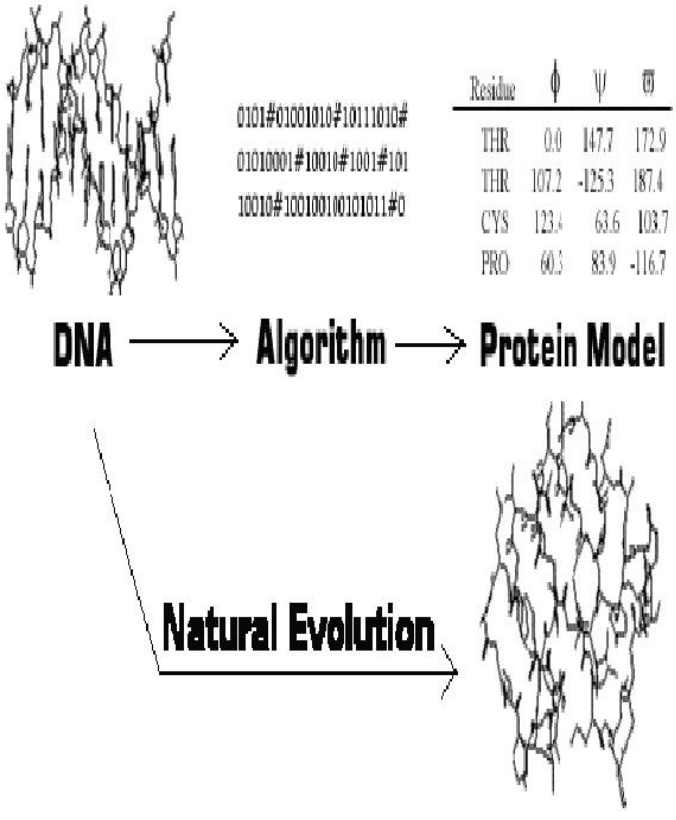


Figure 12: Protein binding targets

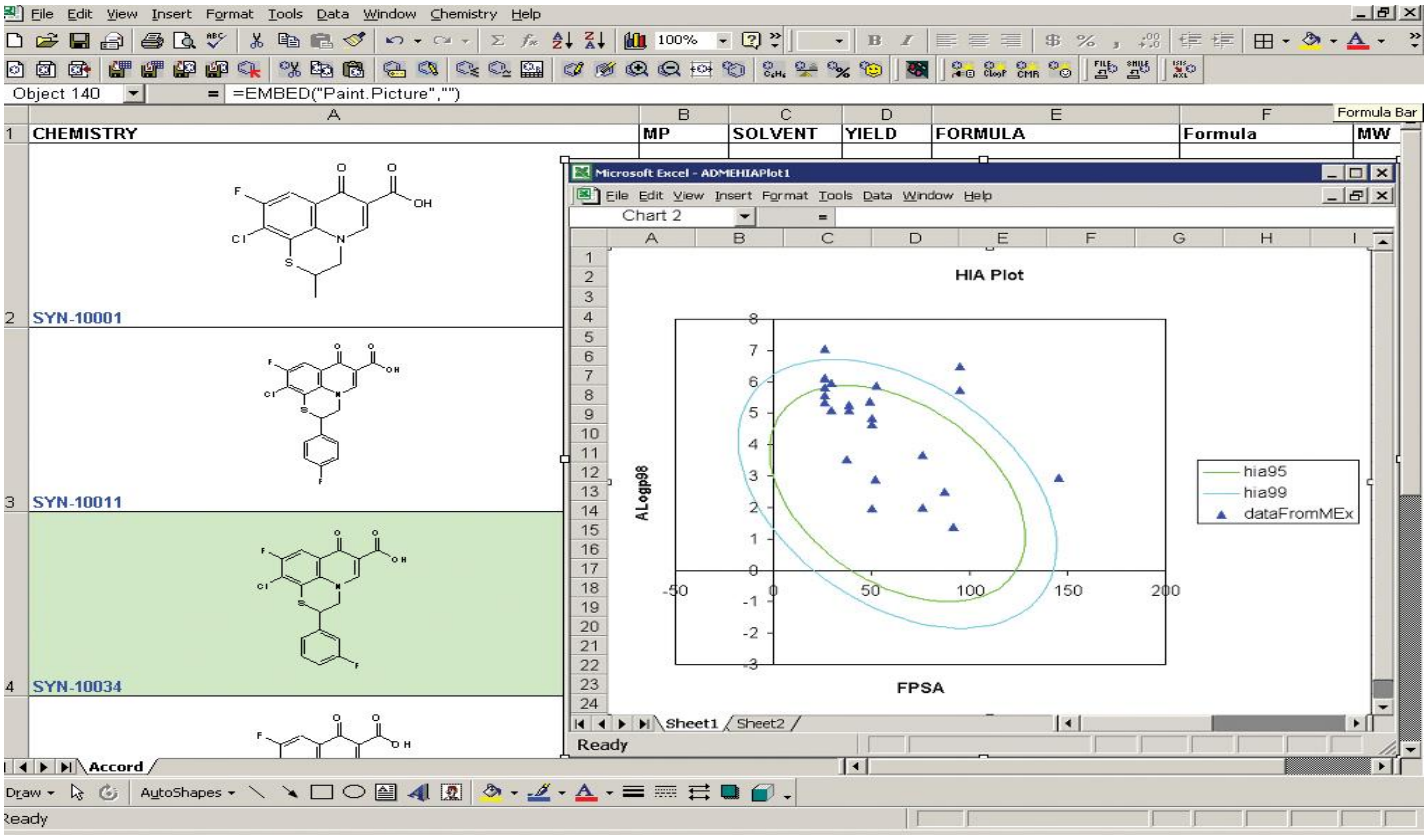


Figure 13: Docking

BIOINFORMATICS SOFTWARES:

MOLECULAR DYNAMICS SOFTWARES:

Abalone (molecular mechanics), AMBER, Ascalaph Designer, Avizo (software), CHARMM, D. E. Shaw Research, Desmond (software), Folding@home, GROMACS, GROMOS, LAMMPS, MacroModel, MDynaMix, Molecular design software, Molecular Modelling Toolkit, NAMD, Tinker (software), Tremolo-X, X-PLOR, XMD, Yasara

MOLECULAR MODELING SOFTWARES:

Abalone (molecular mechanics), AccelrysAscalaph Designer, AutoDock, Avizo (software), Avogadro (software), BALLBOSS (molecular mechanics), Chemical WorkBench, Cn3D, List of computer-assisted organic synthesis software, Cone algorithm, CoNTub, Coot (program), Cresset Biomolecular Discovery, CS-ROSETTA, CYANA (Software), DOCK, EMovie, ESyPred3D, ICM-Browser, Jmol, Khimera, Kintech Lab, Lead Finder, LigandScout, LIGPLOT, Molekel, NOCH, NUPACK, PyMOL, RasMol, Schrödinger (company), Scigress, ShelXle, Simbiosys, Spartan (software), Swiss-model, UCSF Chimera, Yasara, QuteMol

CHEMINFRMATICS SOFTWARES:

AutoNom, CAMEO, The Catalyst, ChemExper, ChemFileBrowser, ChemFinder Pro, Chemkey, ChemProtect, ChemTK Lite, ChemTK, Chiron, emolecules, CIARA, CLiDE, Concord, CORINA, DARC, DayMenus, DTREG, Equbits Insight, JChem, LHASA, MACCS-II, Marvin Applets and Marvin Beans 3.0, Merlin, METEOR, Project Library, REACCS, RS^3 Discovery, SciMetrics, SECS, SMILES Toolkit A, SMOG, SYBYL/3DB UNITY, SYNLIB, Thor, TRIAD, UVSS, Vcharge

CONCLUSION:

Many QSAR/QSPR analyses involve the interactions of a family of molecules with an enzyme or receptor binding site to show the potent molecule. QSAR can also be used to study the interactions between the structural domains of proteins. Protein-protein interactions can be quantitatively analyzed for structural variations resulted from site-directed mutagenesis and by use of this information one can find the exact molecule (Lead Identification), which can fit on the biological receptor platform assumed by the use of bioinformatics, and elicit their action by controlling biochemical malfunction *in-vivo*. The chemistry in the feedback system plays a good role in the correlation between the two info systems as these two are the combination projection if Biochemistry: Bioinformatics-Cheminformatics. There are other things which relate the Cheminformatics and Bioinformatics in the biochemical reactions happen at molecular levels may results into metabolites cause abnormalities or improper functioning of organ and which is under the domain of molecular genomics.

ACKNOWLEDGEMENT:

The author (Vikramkumar Vishnubhai Patel) is very much thankful to the project guide Prof. Dr. Dhrubo Jyoti Sen for allowing him to present his project in oral session of **National Level UG Student Seminar: Pharma Shine 2008**; Sponsored by: Gujarat Council on Science and Technology, Gandhinagar at C.U. Shah College of Pharmacy & Research, Surendranagar, Gujarat, **28 September 2008**. He has bagged first prize in podium.

REFERENCES:

1. Koehn FE and Carter GT; The evolving role of natural products in drug discovery. *Nat. Rev. Drug Discov*.: 4(3), 206–20, 2005.

2. Acharya C, Coop A, Polli JE and Alexander DM; Recent Advances in Ligand-Based Drug Design: Relevance and Utility of the Conformationally Sampled Pharmacophore Approach, *Curr. Comput. Aided Drug Des.*: 1; 7(1), 10–22, 2011.

3. Ghose AK, Viswanadhan VN and Wendoloski JJ; A Knowledge Based Approach in Designing Combinatorial or Medicinal Chemistry Libraries for Drug Discovery: *J. Combin. Chem.*: 1, 55–68, 1999.

4. Clarke FH; How Modern Medicines are discovered. *Future Publishing Company:* 1, 133–157, 1973.

5. Sneader W; Drug Prototypes and Their Exploitation. *John Wiley & Sons*: 1, 564–580, 1996.

6. Bohm HJ, Flohr A and Stahl M; Scaffold hopping, *Drug Discovery Today: Technologies Lead optimization*: 1(3), 217–224, 2004.

7. Sun H, Tawa G and Wallqvist A; Classification of scaffold-hopping approaches, *Drug Discovery Today*: 17(7/8), 310–324, 2012.

8. Hessler Gand Baringhaus KH; The scaffold hopping potential of pharmacophores, *Drug Discovery Today: Technologies*: 7(4), e263–e269, 2010.

9. Sidhu PS, et al.; On scaffold hopping: Challenges in the discovery of sulfated small molecules as mimetics of glycosaminoglycans, *Bioorganic & Medicinal Chemistry Letters:* 23(1), 355–359, 2013.

10. Massarellia I, Macch M, Minutolo F, Prota G and Bianucci AM; QSAR models for predicting enzymatic hydrolysis of new chemical entities in 'soft-drug' design, *Bioorganic & Medicinal Chemistry*: 17, 3543–3556, 2009.

11. Taha MO, Tarairah M, Zalloum H and Abu-Sheikha G; Pharmacophore and QSAR modeling of estrogen receptor β ligands and subsequent validation and *in silico* search for new hits, *Journal of MolecularGraphics and Modeling*: 28, 383–40, 2010.

12. Sakkiah S, Thangapandian S, John S and Lee KW; Pharmacophore based virtual screening, molecular docking studies to design potent heat shock protein 90 inhibitors, *European Journal of Medicinal Chemistry*: 46, 2937-2947, 2011.

13. Kalyaanamoorthy S and Chen YP; Structure-based drug design to augment hit discovery, *Drug Discovery Today*: 16(17/18), 831–839, 2011.

14. Zsoldos Z, Szabo I, Szabo Z and Johnson AP; Software tools for structure based rational drug design, *Journal of Molecular Structure (Theochem)*: 666-667(1), 659–665, 2003.

15. Wlodawer A and Vondrasek J; Inhibitors of HIV-1 protease: a major success of structure-assisted drug design, *Annu. Rev. Biophys. Biomol. Struct*.: 27, 249–284, 1998.

16. Boyd DB; How computational chemistry became important in the pharmaceutical industry., *In Reviews in Computational Chemistry,* 23 Wiley: 401–443, 2007.

17. Rutenber EE and Stroud, RM; Binding of the anticancer drug ZD1694 to *E.coli* thymidylate synthase: assessing specificity and affinity, *Structure*: 4, 1317–1324, 1996.

18. Reddy AS, Pati SP, Kumar PP, Pradeep HN and Sastry GN; Virtual Screening in Drug Discovery – A Computational Perspective, *Current Protein and Peptide Science*: 8, 329-351, 2007.

19. Taylor RD, Jewsbury PJ and Essex JW; A review of protein-small molecule docking methods, *Journal of Computer-Aided Molecular Design*: 16, 151–166, 2002.

20. Bhattacharjee N and Biswas P; Statistical analysis and molecular dynamics simulations of ambivalent α-helices, *BMC Bioinformatics*: 11, 519, 2010.

21. Dodson GG, Lane DP and Verma CS; Molecular simulations of protein dynamics: new windows on mechanisms in biology, *EMBO reports*: 9(2), 144–150, 2008.

22. Moroy G, Martiny VY, et al.; Toward *in-silico* structure-based ADMET prediction in drug discovery, *Drug Discovery Today*: 17(1/2), 44-55, 2012.

23. Colquitt RB, et al; *In-silico* modeling of physiologic systems, *Best Practice & Research Clinical Anesthesiology*: 25, 499–510, 2011.