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FINAL/COMPLETION REPORT

MAJOR RESEARCH PROJECT

MRP F. No.41-472/2012 (SR)

(01.07.2012 to 31.12.2015)

Title of the project

PHARMACOPHORIC ANALYSIS AND DISCOVERY OF NEW DRUGS FROM CYANOBACTERIA

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Annexure-A

(i) BRIEF OBJECTIVE OF THE PROJECT

The present work has been designed and planned to evolve strategy for the identification of potential drugs for various types of cancer through molecular docking with the following objectives.

- To identify the various enzymes causing cancer and to determine the antigenicity of the identified enzymes causing various cancers.
- To find out the possible ligand binding sites from the enzymes.
- To screen the cyanobacterial secondary metabolites available in the database and to identify the effective of cyanobacterial secondary metabolites, acting as a drug, for various cancers through molecular docking.
- To compare the synthetic drugs with cyanobacterial bioactive compounds through molecular docking.

(ii) MATERIALS

In order to analyze anticancer bioactive compounds from cyanobacteria, in the present investigation, cyanobacterial compounds from 20 species such as *Lyngbya* sp, *Lyngbya majuscula, Lyngbya sordida, Lyngbya bouilloni, Lyngbya semiplena, Lyngbya confervoides, Symploca* sp., *Symploca hydnoides, Symploca laete-viridis, Calothrix, Nostoc linckia, Nostoc spongiaeforme, Nostoc sp.* GSV 224, *Nostoc sp. Leptolyngbya sp. Oscillatoria Margaritifera, Phormidium gracile, Phormidium spp.* and *Dichothrix utahensis* from 8 genera bioactive compounds were retrieved form data base (www.chemspider.com).

Various cancers are caused by different kinds of enzymes called receptor molecules. They are Estrogen receptor (ERα) for breast cancer, Epidermal growth factor receptor (EGFR) kinase for lung, Heat Shock protein (HSP90) for skin, brain-type creatine kinase (BB-CK) for brain, bovine lipocalin allergen (BOS D2) for gastric, prostatic acid phosphatase (PAP) for prostate, epidermal growth factor receptor (EGFR) for ovarian, Abelson leukemia tyrosine kinase (ABL) for blood, epidermal growth factor receptor (EGFR) for cervical and

thyroid hormone receptor alpha 1 (THRA1) for thyroid cancer. The receptor molecules, involved in causing the 10 types of cancers, are protein molecules. The above said molecular structures of receptors were retrieved from protein database (www.rcsb.com). To compare the cyanobacterial drugs, the following normally used synthetic drugs against various cancers were selected for the research.

(a) Schrodinger (http://www.schrodinger.com/)

Schrodinger software is drug design software using both ligand and structure-based methods. It provides accurate, reliable, and high performance computational technology to solve real world problems in life science research. It provides superior solutions and services for the design, selection, and optimization of novel drug candidates. Schrödinger's predictive models will enable drug discovery scientists to assess properties of chemical compounds early in the discovery process and to select drug candidates that have optimal profiles. The predictive power of Schrödinger's software allows scientists to accelerate their research and development activities, reduce research costs, and make novel discoveries that might not be possible with other computational or experimental approaches. The various products of Schrodinger are: Glide, Prime, Jaguar, Macro Model, Liaison, QSite, Maestro, LigPrep, Phase, Strike, Induced Fit, SiteMap, Desmond, Impact and Glide.

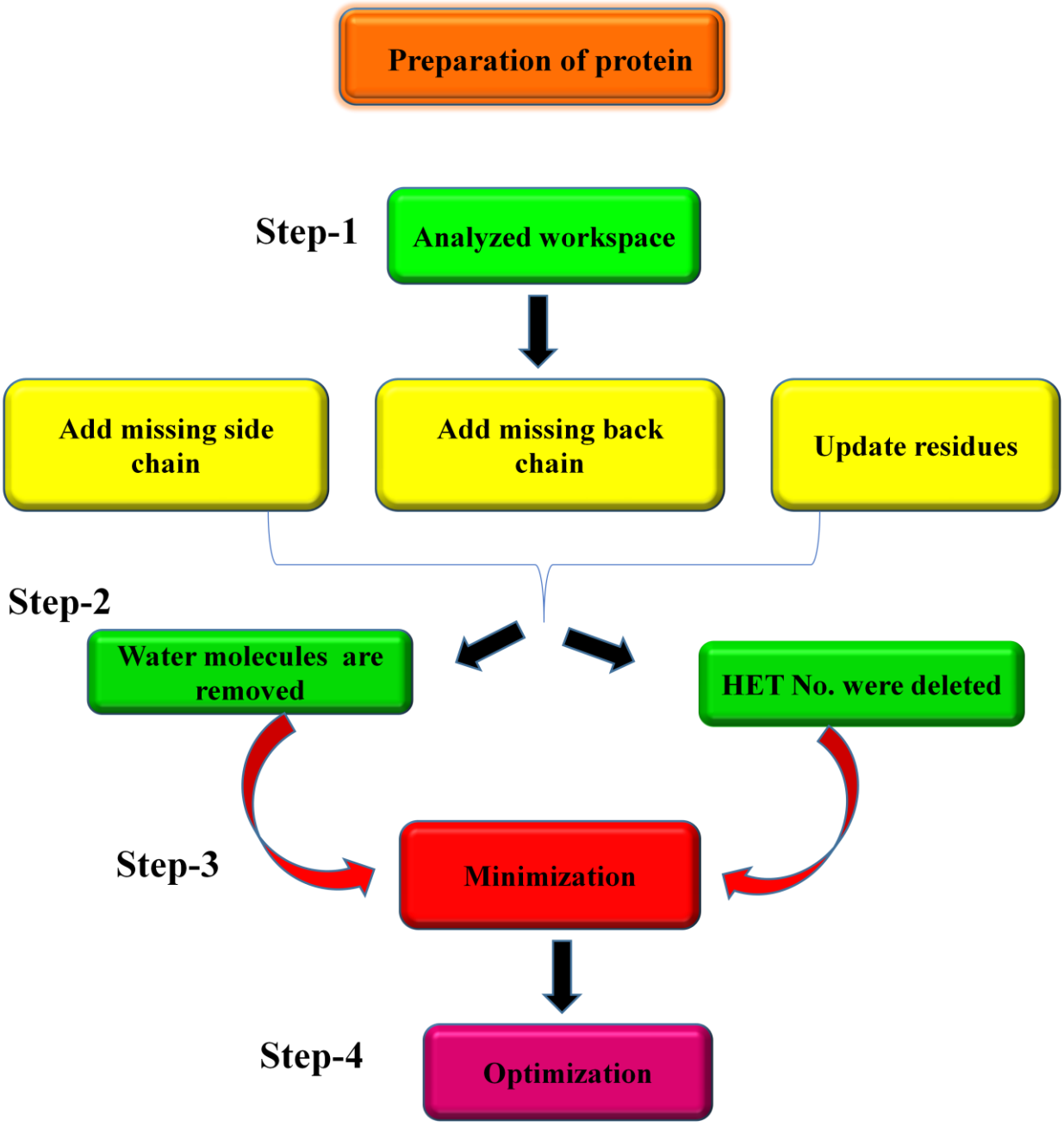
In the present research with the help of Glide, Maestro, LigPrep and SiteMap were used to locate binding sites over the protein molecule and to conduct molecular docking of ligands with the protein molecules.

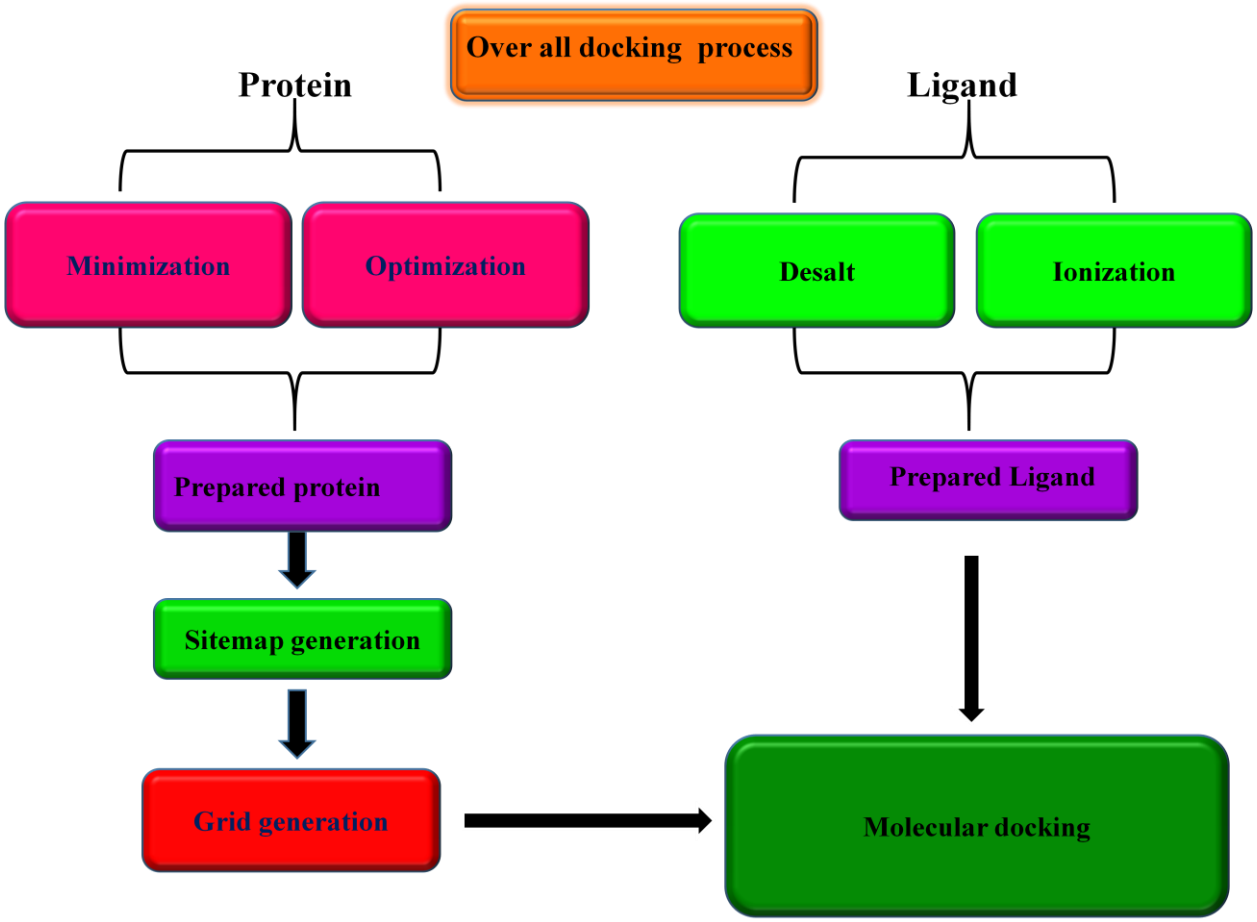
(b) Hex (http://www.hex.loria.fr/dist50/)

Hex is an interactive protein docking and molecular superposition program, written by Ritchie (2008). Hex understands protein and DNA structures in PDB format, and it can also read small-molecule SDF files. Using Hex software, protein-protein and protein-ligand docking are possible. In this docking one molecule (always protein) acts as receptor and the

other as ligand. Hex will run on most Windows-XP, Linux and Mac OS X PCs. The latest Intel and Mac versions have been built for Ubuntu 9.4 and 9.10. All of these versions now include CUDA support for Nvidia GPUs. Earlier Intel PC versions are available for Fedora Core 4 and 6, RedHat 9, and Ubuntu 7.01. Binaries for earlier versions are available for Sun and Silicon Graphics workstations. The Protein-Ligand interaction plays a significant role in structural based drug designing. In the present study ten different cancers causing proteins selected as receptors and the commercially available drugs selected as ligands.

METHODOLOGY OF SCHRODINGER SUITE




Over all docking process
Protein
Ligand
Minimization
Optimization
Desalt
Ionization
Prepared protein
Prepared Ligand
Sitemap generation
Grid generation
Molecular docking

(iii) WORK DONE AND RESULTS ACHIEVED

(a). Breast cancer

Breast cancer is a type of cancer originating from breast tissue, most commonly from the inner lining of milk ducts or the lobules that supply the ducts with milk. ERα, plays an important role in breast cancer development by mediating estrogen induced cell proliferation. In breast cancer, ERαis to be controlled by effective anti tumor compounds. Therefore, in the present investigation, suitable drug molecules with high binding affinity, which could be possible lead molecules, are to be predicted.

Out of 272 cyanobacterial bioactive compounds, 135 showed docking responses against the receptor causing breast cancer which showed Glide scores ranging from -1.735733 to - 10.81373. The top two scorers, cryptophycin-F with -10.81373 and cryptopycin-G with - 9.50125, were selected as the best bioactive compounds to act against ERα. Hence, cryptophycin-F and cryptopycin-G were selected as cyanobacterial anticancer drugs for breast cancer. In addition to the above two drugs, currently used synthetic drugs, such as raloxifene and toremifene were also taken into consideration for the identification of most effective drug.

Molecular docking

In order to find out the best effective drug, Hex docking was carried out. In this docking, two cyanobacterial bioactive compounds along with two synthetic drugs were taken into consideration for docking as ligand molecules. These ligands have been used to target ERα which bound to the receptor to inhibit its function. The nature of the complex between the drug and the receptor molecule was identified via docking and the inhibition nature of the ligands and their binding affinities were calculated using free energy simulations.

Docking results between ERαreceptor and the synthetic (raloxifene and toremifene) and cyanobacterial drugs (cryptophycin-F and cryptopycin-G) were tabulated. In this study, cryptophycin-F showed a maximum e-value (-319.11) followed by cryptopycin-G (-267.86),

raloxifene (-282.91) and toremifene (-248.61) (Table.14). When comparing the synthetic drugs currently used for the treatment, cryptophycin-F, a compound of cyanobacterial origin, is considered to be better and more effective drug in treating the ERαreceptor causing breast cancer. Hence the cryptophycin-F molecule showed a high binding affinity with the major active site of receptor molecule ERα, it is clear that the cyanobacterial drug cryptophycin-F could be used as an effective drug in combating ERαcausing breast cancer.

(b). Lung cancer

Lung cancer is characterized by uncontrolled cell growth in the tissues of the lungs and nearby tissues or other parts of the body caused by Epidermal Growth Factor Receptor (EGFR) kinase.

Cyanobacterial bioactive compounds (drug molecules)

Currently, for cancer treatment, adequate potent medicines are not available. Marine cyanobacteria are considered to be the potential organisms with rich source of known and novel bioactive compounds, which are effective in either killing the cancer cells or affecting the cells signaling for cancer. Among the various members of marine cyanobacteria, 9 species such as *Calothrix sp.*, *Lyngbya confervoides*, *L.majuscula*, *L.sordida*, *Lyngbya sp*., *Nostoc sp*., *Phormidium gracile*, *Symploca hydnoides* and *Symploca sp*. are considered to be highly potential organisms having 33 bioactive compounds. These bioactive compounds when docked against receptor molecule, EGFR kinase by Glide module (Schrodinger suite), tiglicamide-A and symplocamide-A were selected as they showed a strong interaction and binding with target proteins having best docking scores when compared to other tested ligands. Based on the results of the present study it can be concluded that the drugs tiglicamide-A and symplocamide-A are very effective anticancer drugs against lung cancer.

From these results, it is concluded that among the various cyanobacterial anticancer compounds, two top scorers, tiglicamide-A (-10.485) and symplocamide-A (-7.962) were

identified as the best ligand molecules against lung cancer. Currently, cabazitaxel and apraclonidine are used as synthetic lung cancer drugs. In order to find out the most effective drug among the four, molecular docking was carried out using Hex software.

Molecular docking

In molecular docking using Hex, commercially available synthetic drugs and cyanobacterial bioactive compounds were targeted against EGFR kinase. The active ligand binding site of the receptor, EGFR kinase, is lined with 16 amino acids of which 8 were hydrophobic. These hydrophobic amino acids play an important role in molecular interaction during docking. Among the four drugs, tiglicamide-A was found to be the most effective drug against lung cancer as it showed a maximum e-value -434.01 against molecule causing lung cancer followed by symplocamide-A with -420.83, cabazitaxel and apraclonidine with -332.35 and -175.91. Hence, the tiglicamide-A was identified as the best ligand molecule against EGFR kinase.

(c). Skin cancer

Skin cancer is growing as a dreadful human disease as compared to other cancers and the various types of skin cancers are named based on the type of skin cell from which they arise. Basal cell cancer originates from the lowest layer of the epidermis; squamous cell cancer originates from the middle layer, and melanoma, which originates in the pigment-producing cells, melanocytes.

Drug molecules

Among the various members of marine cyanobacteria tested, *Lyngbya majuscula*, *L. sordida*, *L.confervoides*, *Lyngbya sp*., *Calothrix*, *Nostoc sp*., *Phormidium gracile*, , *Symploca hydnoides* and *Symploca sp*. are highly potential organisms which have anticancer drug molecules such as antillatoxin-B, apratoxin-C1, arulide-C, baslynbiyaside, belamide-A, calothrixin-B, caylobolide-A, cryptophycin-6, kemopeptinde-B, hoamide-D1, homodolastin,

isomalgamide-B, lagunamide-A1, lynbyabelin-I, lynbaysolide-1, lyngbastatin, majusculamide-D, maleviamide-D, malyngamide-P, 2epi malyngolide, nostocylopeptide, obynanamide, pitipeptolide-B, pitiprolamide, somocystinamide, symplocamide-A1, symplostatin-2, tasipeptin-B, tasiamide-B, tiglicamide-B and veraguamide-L. To screen the above bioactive compounds against skin cancer causing protein, HSP90, Glide module (Schrodinger suite) was applied. Of the bioactive compounds tested, tasiamide-B from *Symploca* sp and lyngbyastatin-4 from *L. confervoides* were identified as the best drugs based on their Glide scores such as -9.144 and - 8.515. These two cyanobacterial drugs were compared, for their efficiency, with the synthetic drugs like cabazitaxel and dyclonine through molecular docking using Hex.

Molecular docking

Totally four drugs such as cabazitaxel, dyclonine (synthetic), tasiamide-B and lyngbyastatin-4 (cyanobacterial) were tested for their performance against HSP90 using Hex software. Among the four, the cyanobacterial drug, tasiamide-B was found to be more potential in having a maximum e-value –358.20 (Table.14) followed by lyngbyastatin-4 (-353.14), cabazitaxel (-294.2) and dyclonine (-216.16).

During the docking process of the ligand molecule (tasiamide-B) was at the centre of the active binding site. The cavity of the active binding site was lined with 17 amino acids of which 7 were hydrophobic, 4 polar, 3 with negative charge, 2 glycine and the remaining one was lyscine. Due to the position of the ligand at the centre of the cavity and the arrangement of amino acids in the binding site, the interaction is more effective. Thus it is concluded that the molecular docking between the receptor molecule HSP90 with the ligand molecule tasiamide-B was more effective.

(d). Brain cancer

The brain cancer includes tumors inside the cranium or in the central spinal canal.

Drug molecules

Out of 272 cyanobacterial bioactive compounds, 221 molecules were identified to interact with the receptor molecule, Brain-type creatine kinase enzyme (BB-CK). In the present study, Glide module docking method was used for the prediction of bioactive compounds from cyanobacteria. The Glide score of tested 221 bioactive compounds was ranging from -0.690132 to -9.336775. Among them, lyngbyastatin-2 from *L. majuscula* and symplocamide-A from *Symploca* sp. showed maximum Glide scores, -9.3368 and -8.6387. Totally, four ligands, two from cyanobacteria (symplocamide-A and lyngbyastatin-2) and two synthetic drugs (temozolomide and afinitor) were selected for further study.

Molecular docking

Molecular docking was carried out using Hex software to find out most efficint ligand. Among the four, symplocamide-A and lyngbyastatin-2, from cyanobacteria showed highest scores, -341.33 and -350.80 respectively. Of the two cyanobacterial drugs, lyngbyastatin-2 was identified as the most potential cyanobacterial drug as it recorded the highest Hex score (-350.80). The synthetic drugs, temozolomide and afinitor, recorded the least scores, -190.53 and - 260.16.

The recognition and affinity of ligand towards receptor is observed at the active binding site. The pocket of the active site is surrounded by 26 amino acid residues, of which, 9 of them are hydrophobic, 10 charged positive. 4 polar and 3 charged negative. The high affinity of BB-CK towards lyngbyastatin-2 is favoured by three hydrogen bonds, formed by Leu-193, His-191 and Lys-196. The docking study reveals that van der Waals forces play an important role in stabilizing the receptor-ligand complex. The van der Waals interaction and hydrogen bonding formed by the reactive amino acid residues of the receptor lead to binding

of receptor molecule with lyngbyastatin-2. Hence the cyanobacterial drug, lyngbyastatin-2 was selected as the best drug for brain cancer.

(e). Gastric cancer

Gastric cancer is arising from any part of the stomach. It is difficult to cure this cancer unless it is identified in early stages.

Drug molecules for gastric cancer

The screening of cyanobacterial bioactive compounds was carried out using Glide program. These compounds were made to dock with the receptor molecule to find out the binding efficiency in the form of Glide score. Out of 272 bioactive compounds, only 122 were interacted with the receptor BOS D2. The Glide score of 122 compounds is ranging from - 1.642561 to -6.464462. From these compounds, two top scorers, lyngbyastatin-7 and lyngbyastatin-2 with Glide scores -6.464462 and -6.462055 respectively were selected to act as ligands against BOS D2. Synthetic drugs, capecitabine and doxorubicin were also taken for docking study using Hex software.

Molecular Docking

The four ligand molecules, lyngbyastatin-7, lyngbyastatin-2, capecitabine and doxorubicin, were targeted against BOS D 2 in the molecular docking study using Hex. Among the four molecules, two cyanobacterial compounds lyngbyastatin-7 and lyngbyastatin-2 recorded the highest e-value scores -402.14 and -419.12 respectively. On the other hand, the synthetic drugs, capecitabine and doxorubicin, showed lesser energy values -253.60 and -299.16.

In the molecular interaction study, the active binding site of BOS-D2 is lined with 13 amino acids from which 7 of them are hydrophobic, 3 charged negative, two polar and one glycine. Among the bioactive compounds, lyngbyastatin-2 is located at the centre of the cavity surrounded by 13 amino acid residues in the binding site resulting with highest binding

score, -419.12 and hence this compound is identified as the best drug for the treatment of gastric cancer. Since lyngbyastatin-2 showed the highest e-value over the other cyanobacterial drug, it was selected as the effective drug molecule against BOS D2 receptor.

(f). Prostate Cancer

Prostate cancer is a form of cancer that develops in the prostate gland in the male reproductive system. It causes pain, difficulty in urinating and problems during sexual intercourse.

Molecular docking

Molecular docking through Hex was carried out with four ligand molecules, lyngbyastatin-2 and tiglicamide-A (cyanobacterial compounds), cabazataxel and docetaxel (synthetic drugs) against PAP. Among the four, lyngbyastatin-2 recorded the highest e-score, - 509.63 while the remaining three molecules showed only lesser energy compared to lyngbyastatin-2.

During molecular docking, chemical interactions between lyngbyastatin-2 and the active binding site of PAP were observed. The cavity of the active binding site is surrounded by 27 amino acid residues. Among them, 10 were hydrophobic, 5 positively charged, 4 negatively charged and 8 were polar. Four hydrogen bonding between ligand and the surrounding amino acid residues were observed. The position of the ligand molecule was at the centre of the active binding site. Therefore, the cyanobacterial compound lyngbyastatin-2 was selected as the best drug molecule to act against PAP receptor.

(g). Ovarian cancer

Ovarian cancer is a cancerous growth arising from the epithelium of the ovary and the fallopian tubes.

Molecular docking

To identify the best active molecule against EGFR, carboplatin and cisplatin (synthetic drugs), lynbyastatin-4 and lyngbyastatin-2 (cyanobacterial drugs) were subjected to molecular docking using Hex software. In the docking, the e-values obtained were -156.48, -175.18, - 446.67 and -541.40 for carboplatin, Cisplatin, lynbyastatin-4 and lyngbyastatin-2. Among these, lyngbyastatin-2 showed the highest energy value and hence this compound was selected as the best cyanobacterial bioactive compound for ovarian cancer.

The active binding site of the receptor, EGFR molecule is lined with 22 amino acids from which 20 of them are hydrophobic, 2 polar and with three hydrogen bonds. In this case also, effective chemical interaction takes place between protein and ligand molecule through the van der Waals forces, electrostatic and hydrogen bonding. From the above study, lyngbyastatin-2 was predicted as the best drug against EGFR.

(h). Blood Cancer

Blood cancer is caused by malignancy in the blood, lymphatic system and bone marrow. Blood cancer starts in the bone marrow, where blood is produced, and affects the normal production and function of the blood cells.

Molecular docking

To identify the best effective drug molecule against ABL tyrosine kinase, molecular docking using Hex software was performed between ABL tyrosine kinase and the selected four ligand molecules. During docking, effective binding was observed between Lyngbyabellin D1 and ABL tyrosine kinase resulting in highest docking score, - 349.91, while the other three ligand molecules exhibited less energy values such as -278.53, -202.93 and -290.10 for Ponatinib, Synribo and Cryptopycin-F.

In the molecular interaction process, the high affinity of the ABL tyrosine kinase towards lyngbyabellin-D1 was observed due to the presence of four hydrogen bonding

formed by Asn 83, Glu 142, Gly 201 and Arg 180 in the binding site of receptor with ligand molecule lyngbyabellin-D1. The active binding site of receptor is lined with 33 amino acids from which 13 are hydrophobic, 3 charged negative, 10 polar, 5glycine and one with positive charge showing n-cation. Van der Waals forces and electrostatic attraction play an important role in stabilizing the protein-ligand complex which caused higher docking score for lyngbyabellin-D1 over the other ligands. From this research, it is concluded that lyngbyabellin-D1 was identified as the best drug for the treatment of ABL tyrosine kinase induced blood cancer. Therefore based on e- value, it is concluded that lynbaybellin D1 is the effective drug molecule against blood cancer.

(i). Cervical cancer

Cervical cancer is a malignant neoplasm arising from cells originating in the cervix of the uterus. One of the most common symptoms of cervical cancer is abnormal vaginal bleeding.

Drug molecule

Glide docking was carried out to screen the cyanobacterial bioactive compounds to act as drugs against cervical cancer. Among the 272 compounds, 213 showed docking response to the receptor EGFR and the docking scores are tabulated. The two top scorers, symplocamide-A1 (-10.117783) and tasiamide-B (-8.953288) were identified as the most effective cyanobacterial drugs. To compare the efficiency cyanobacterial drugs, with synthetic drugs, commonly used, such as blenoxane and hycamtin were selected. Thus two cyanobacterial and two synthetic drugs were selected for the study.

Molecular docking

To identify the best drug molecule against the receptor, EGFR, causing cervical cancer, molecular docking, using Hex software, was carried out. In this analysis, the cyanobacterial ligand, symplocamide-A1 showed the highest e-value -461.21 followed by

tasiamide-B (-446.37), blenoxane (–420.97) and hycamtin (-304.69).

During docking between symplocamide-A1 and EGFR, perfect binding was observed. The active binding site is surrounded by 19 amino acid residues in which 11 are hydrophobic, one negatively charged, 4 polar, 2 with positively charged and one is glycine. The ligand molecule is located at the centre of the binding site which leads to the effective binding between the receptor and ligand. From the docking interaction, it is observed that the van der Waals forces play an important role in stabilizing the protein-ligand complex which resulted in higher docking score.

From the above study, it is concluded that the cyanobacterial bioactive compound, symplocamide-A1 was identified as the best effective drug molecule, based on docking score, for treating the cervical cancer.

(j). Thyroid cancer

Thyroid cancer is a malignant neoplasm originating from follicular or para follicular thyroid cells.

Drug molecules for thyroid cancer

In cyanobacteria, out of 272 bioactive compounds after screening by Glide docking, 200 bioactive compounds showed response towards thyroid receptor molecule. The Glide score was ranging from -0.877399 to -6.482245. Among the 200 molecules, top two scorers, lynbyastatin-4 (-6.440504) and pompanopeptin-B (-6.482245) were selected as the ligand molecules based on the highest Glide scores obtained. To compare the efficiency of cyanobacterial bioactive compounds, commonly used synthetic drugs such as cabozantinib-S-Malate and vandetanib were also used as ligands in Hex docking.

Molecular docking

The four ligand molecules, two each from cyanobacteria and synthetic drugs, were taken into consideration for the molecular docking using Hex software. These four ligands,

two from cyanobacteria (lynbyastatin-4 and pompanopeptin-B) and the other two from synthetic drugs (cabozantinib-S-Malate and vandetanib) were docked against the receptor molecule, THRA1 causing thyroid cancer. In the molecular docking, pompanopeptin-B showed highest score (-432.61) indicating its most effective nature. The other three molecules showed scores less than that of pompanopeptin-B (lynbyastatin-4 -305.25, cabozantinib-S-Malate-302.35 and vandetanib-252.21). Thus, among the four ligands, pompanopeptin-B was selected as the best cyanobacterial drug molecule for treating thyroid cancer.

The receptor molecule THRA1 interacts with pompanopeptin-B during molecular docking. The recognition and affinity of ligands towards protein is interpreted by the inter-atomic distances and hydrogen bonding formed between the amino acid residues of docked protein-ligand complex. The prominent binding pockets were identified using Glide module. The pocket of the active site is surrounded by 20 amino acids from which 14 of them are hydrophobic, 4 polar, 1 Glycine and another one charged positive. The high affinity of the receptor towards pompanopeptin-B is favored by four hydrogen bonds. The docking study reveals that van der Waals forces play an important role in stabilizing the protein-ligand complex. These forces and hydrogen bonds formed by the reactive amino acid residues of the receptor with the ligand molecule leads to effective binding of receptor molecule with pompanopeptin-B. From the above results it is clear that the pompanopeptin-B is best drug molecule against thyroid cancer. When ten kinds of receptors, causing ten different types of cancers, were made to dock with cyanobacterial and synthetic drugs, the cyanobacterial drugs were found to be the most effective when compared to synthetic drugs. Among the 272 bioactive compounds, through Glide dock and Hex, seven compounds were predicted as effective drugs for the treatment of ten kinds of cancers. Among them, lyngbyastatin-2 was predicted as the best effective drug against brain, gastric, prostate and ovarian cancers. The remaining drugs such as cryptopycin-F, tiglicamide-A, tasiamide-B, lynbaybellin-D1,

symplocamide-A and pompanopeptin-B, were found to be effective for breast, lung, skin, blood, cervical and thyroid cancer. All the above discussed materials are found to be suitable drug candidates for cancer and **the obtained results are published in reputed refereed science citation indexed international journals given below with proper acknowledgement for the financial support given by University Grants Commission under this Major Project F. No.41-472/2012 (SR) & 1.7. 2012**

Annexure-B

(iv) SUMMARY OF THE FINDINGS

Ten different types of cancer such as breast, lung, skin, brain, gastric, prostate, ovarian, blood, cervical and thyroid are more common in human beings. Enzymes, causing cancers, like Estrogen receptor (ERα) for breast cancer, Epidermal Growth Factor Receptor (EGFR) kinase for lung , Heat Shock protein (HSP90) for skin, Brain-type creatine kinase enzyme (BB-CK) for brain, Bovine lipocalin allergen (BOS D2) for gastric, Prostatic acid phosphatase (PAP) for prostate, Epidermal Growth Factor Receptor (EGFR) for ovarian, Abelson leukemia Tyrosine Kinase (ABL) for blood, epidermal growth factor receptor (EGFR) for cervical and Thyroid Hormone Receptor Alpha 1 (THRA1) for thyroid cancer were selected for the study. These enzymes were screened for antigenicity, using TMHMM, and were found to be effective antigens to induce tumors. All the enzymes showed 10 possible ligand binding sites on their surface. Among the 10 binding sites, only one acted as active binding site.

For treating cancer, 272 analogues of 52 cyanobacterial bioactive compounds from 20 different species, belonging to 8 genera, were screened through Glide docking with ten different receptors causing cancers.

Out of 272 cyanobacterial bioactive compounds, 135 for breast, 209 for lungs, 217 for skin, 221 for brain, 122 for gastric, 220 for prostate, 207 for ovarian, 191 for blood, 213 for cervical and 200 for thyroid cancers were screened for their docking ability with the receptors. Best two bioactive compounds for each receptor, having highest glide scores were selected to act as drugs (ligands) for Hex docking study. Two synthetic drugs for each cancer and the above two bioactive compounds were made to dock with each receptor molecule using Hex, and energy values were obtained. From the Hex docking, 7 cyanobacterial

bioactive compounds such as lyngbyastatin-2, tiglicamide-A, cryptopycin-F, pompanopeptin-B, lynbaybellin-D1, symplocamide-A and tasiamide-B were selected based on the highest e-value obtained. Of the seven ligands identified from cyanobacteria, 3 were from *Lyngbya confervoides*, 2 from *Symploca sp* and one each from *Lyngbya majuscula* and *Nostoc spp.*

Among them, lyngbyastatin-2 from *Lyngbya majuscula* was predicted as the best effective drug against brain, ovarian, prostate and gastric cancers. The remaining drugs such as tiglicamide-A, cryptopycin-F, pompanopeptin-B, lynbaybellin-D1, symplocamide-A and tasiamide-B were found to be effective for lungs, breast, thyroid, blood, cervical and skin cancer.

CONTRIBUTION TO THE SOCIETY

Cyanobacteria constitute a unique group of oxygenic photosynthetic bacteria and populate diverse habitats throughout the world. Their potential as a good source of new therapeutic lead compounds has been realized during the past two decades, as several bioactive molecules obtained from cyanobacteria show a broad spectrum of activities, such as antitumor, antibacterial, and antiviral effects, and protease inhibition. Another advantage of cyanobacteria as a microbial source for drug discovery lies in the economy of their cultivation compared with other microorganisms, as the former require only simple inorganic nutrients for growth. Thus, it seems that the cyanobacteria have the potential for expanded utilization in drug discovery. Further, owing to a high degree of microbial diversity, cyanobacterial secondary metabolites may constitute a prolific source of new entities leading to the development of new pharmaceuticals. Yet, exploitation of the cyanophycean species has been hampered by a number of issues related to their handling. With most of these problems having been resolved now, cyanobacteria have the potential to expand the variety of natural products obtained from microorganisms. The relative disregard of cyanobacteria in

the past compared with other microbial sources of natural products, as well as the huge chemical diversity and biological activities of their products, has made them attractive sources of novel drugs for use in diverse therapeutic areas. Hence, pharmaceutical potential of cyanobacteria deserves more scientific attention and interdisciplinary research, and cyanobacterial strains from still unexplored and extreme habitats can serve as good candidates in this regard.

List of Publications

S.No	Bibliography	Publisher	Impact factor	Citation as on 31.12.2015
1.	**Vijaykumar, S.,** Menagha M, 2013 Biomedicine and Preventive Nutrition. 4,355 – 358.	Elsevier	0.442	2
2.	Sangeetha, M., Menagha, M., **Vijaykumar, S.,** 2014 Journal of Biome and Pre Nutrition. 4, 71 – 73.	Elsevier	0.442	1
3.	**Vijaykumar, S.,** Menagha, M., 2014 Biomedicine and Aging Pathology. 65 - 70.	Elsevier	0.734	5
4.	Madhumathi. V., **Vijaykumar S.** 2014. BMR *Bioinformatics & Cheminformatics*. 1, 1-6.	BMR	0.431	2
5.	**Vijaykumar. S.,** Ramesh. V., 2014. Asian Pacific Journal of Tropical Disease. 670 – 674.	Elsevier	0.581	1
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9.	J.E. Movin yabesh, S. Prabhu and **S. Vijayakumar** (2014). Journal of Ethnopharmacology 154; 774-789.	Elsevier	2.998	18
10.	Rambabu, V., Suba, S., **Vijayakumar, S**., 2015. Journal of Pharmaceutical analysis 5 378–382.	Elsevier	0.921.	3
11	Vijayakumar, S., Menagha, M., 2015. Pharmaceutical application of cyanobacterial - A review. Journal of Acute Medicine 5, 15-23.	Elsevier	0.731	1
12	Ramesh, V., **Vijayakumar, S.** 2015. Asian Pacific Journal of Tropical Disease S47-S50.	Elsevier	0.581	2
13	Ramesh, V. **Vijayakumar, S**. 2015. Asian Pacific Journal of Tropical Disease 5(1). IF: 0.	Elsevier	0.581	2
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