REVIEW PUBLIC HEALTH

North Clin Istanb 2024;11(1):171–176
doi: 10.14744/nci.2023.87523

# Bioinformatics approach for searching for natural products in vector-borne disease management

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## ABSTRACT

Vector-borne disease is an important public health problem. This disease is common in tropical areas and affects millions of people. The control and management of disease is an important consideration. Effective treatment is important in management of patients infected with vector-borne disease. A common problem in therapeutic management of the patient is the lack of an effective drug. Therefore, it is necessary to find a new effective drug for managing vector-borne disease. To search for a new drug, new technologies are applicable. Bioinformatics technologies are useful in new drug search. Application of the bioinformatics technologies in new anti-vector-borne disease drug search is interesting. In this review, the author briefly discusses the use of bioinformatics technology in searching for natural products in vector-borne disease management. Concepts and examples of some important diseases are presented.

*Keywords: Bioinformatics; drug; search; vector-borne disease.*

***Cite this article as:*** *Mungmunpuntipantip R, Wiwanitkit V. Bioinformatics approach for searching for natural products in vector-borne disease management. North Clin Istanb 2024;11(2):171–176.*

Vector-borne disease is a group of medical disorders caused by vectors. It is an important public health problem. Vector-borne disease is common in tropical areas and affects millions of people [1, 2]. The disease has a wide clinical spectrum and can result in fatality. The control and management of the disease is an important consideration in global public health. Early diagnosis and prompt treatment are necessary for managing of a vector-borne disease.

Effective treatment is important in successful management of the patient infected with a vector-borne pathogen. At present, a common problem in therapeutic management of the patient is the lack of an effective drug. Hence, it is necessary to find a new effective drug for managing vector-borne disease. To search for a new drug, there are many new useful technologies. Bioinformatics technologies are applicable for new drug searches. Application of bioinformatics technologies for searching for new anti-vector-borne disease drugs is interesting. In this review, the author briefly discusses how bioinformatics technologies are applicable for searching for natural products that might be useful for vector-borne disease management. Important concepts and examples of some important vector-borne diseases are presented.

*Received:* March 09, 2023 *Accepted:* May 05, 2023 *Online:* April 25, 2024

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## How Can Bioinformatics be Useful for Infectious Disease Treatment?

Bioinformatics was first described in 1988 by Lim H. Lim described bioinformatics as "a collective term for data compilation, organisation, analysis and dissemination", which is an application of information technology to help solve biological problems. Bioinformatics emerged after the completion of the genome project [3]. The influx of data led to requirement of new technologies for data manipulation, interpretation and clinical application. Bioinformatics is the new science that links biological and computational sciences [4]. The new hybrid science has become useful in medicine for many years.

Many molecular biological analyser, innovative computational software and databases are useful for clarifying and predicting complex biological phenomena. Analysis of data by bioinformatics becomes a useful biomedical discipline in the post-genomics era.

### Highlight key points

- Vector-borne infection disease is still the important public health problem in many countries.
- Several natural products are proposed for their possible advantage in management of vector-borne disease.
- Bioinformatics technique can be useful in searching for natural products that have anti-vector-borne disease characteristics.

There are many ways that bioinformatics might be applied in medicine [5]. In infectious medicine, several bioinformatics technologies are useful for diagnosis, treatment and prevention of diseases (Table 1) [5–13].

## Natural Products in Vector-Borne Disease Management

Natural product is usually the target for new drug search. Many classical drugs in classical alternative medicine are classified as natural products. The role of traditional natural products, such as herbs, in management of tropical

**Table 1.** Important bioinformatics techniques and application in management of infectious disease [5]

| Bioinformatics techniques | Details |
|---|---|
| Database search | Database is useful for collection of scientific data. Many databases are useful for new drug candidate identification. Database construction and search is usually the first step of bioinformatics drug searching. |
| Genomics | Genomics is an analysis of gene and transcript within the genome and is an early step of bioinformatics analysis [6, 7]. There are many genomics methods that can help with gene finding analyses. Many genomics tools are online available and free for use. The genomics can help clarify genomic background of pathogen and help compare between pathogens.<br>For new emerging infection, genomics can help trace the origin of pathogen via phylogenomic approach. Additionally, genomics analysis can help predict new mutant of the pathogen. |
| Proteomics | Proteomics can help clarify protein structure based on its amino acid code. Similar to genomics, comparative proteomics can help homology analysis and tracing for divergent evolution of proteins [8, 9]. This is useful for tracking the evolution pathway of focused pathogen and help search for new drug targets. Structural proteomics technique can help analyze NMR and X-ray crystallography data. Identification of drug interaction within molecule is possible and thee process is useful for further interaction analysis. |
| Expressional analysis | Basic gene ontology analysis is useful for expressional analysis. Biological process, molecular function and cellular component prediction is based on gene ontology. Derived data are appliacable for further study on interaction of molecules [10, 11]. In silico mutation and hybridization can be simulated [12, 13]. |
| Chemoinformatics | Chemoinformatics involves in the design, creation, organisation, management, retrieval, analysis, dissemination, visualization and use of chemical information. Structural prediction, substructure search and similarity analysis of chemicals are useful for pharmaceutical application [5]. |
| Immunoinformatics | Immunoinformatics is useful for epitope identification. Either B cell or T cell epoitope can be predicted. In silico computational design for new vaccine candidate is possible. |
| Interaction analysis | Interaction analysis via interactomics is possible. In silico molecular docking is possible and is useful for predicting pharmacological reaction of new drug. |

TABLE 2. Important vector borne diseases and possible useful natural products for disease management

| Diseases | Details |
|---|---|
| Malaria | Malaria is one of the most important vector borne diseases caused by Plasmodium parasite. Herbs are well described for usefulness in malarial treatment. Artemisin and artemisinin are two important drug developed from Chinese herb [15, 16]. *Artemisia annua* is the herb that is original natural product for development of the two mentioned new antimalarial drugs [16]. |
| Dengue | Dengue is another important vector borne disease. The standard treatment for dengue is fluid replacement therapy. Some natural products are proposed for possible usefulness in management of dengue. *Kaempferia galanga L* is an example of well-known traditional herb that is mentioned for its usefulness is dengue treatment [17]. |
| Chikungunya | Chikungunya is another important vector borne disease. Andrographolide is a natural product derived from a traditional herb namely *Andrographis paniculata*. It is mentioned for its usefulness against chikungunya virus infection [18]. |
| Zika virus infection | Zika virus infection is a new emerging vector borne disease. Active drug search is important. There are some new reports on using herbal natural products for treatment of Zika virus infections. The good example of natural product is leaves of *Ocimum basilicum* [19]. |

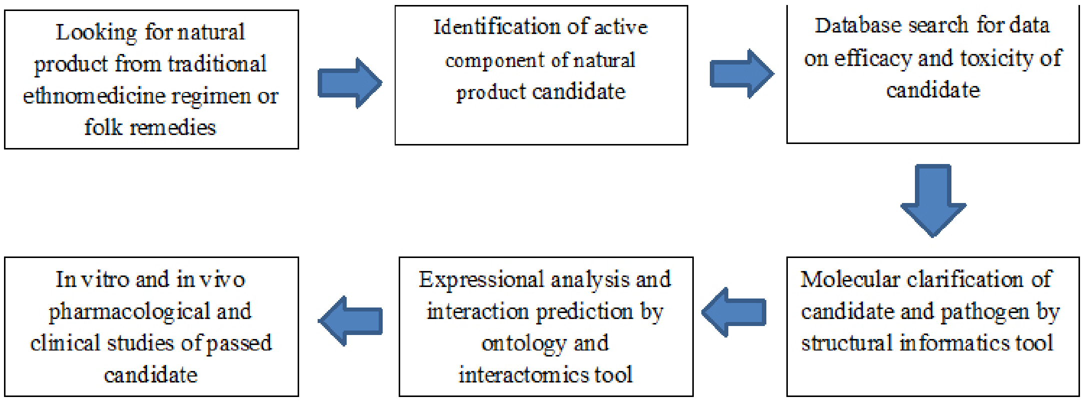

FIGURE 1. Steps for using informatics tool for searching for natural products in vector-borne disease management.

Figure by Wiwanitkit, 2021

vector-borne disease is very interesting. There are many ongoing researches on traditional herb effect on several tropical infections including vector-borne disease.

The well-known natural products proposed for their usefulness in management of vector-borne diseases include herbs and animal products. In traditional medicine, many herbs are mentioned for clinical usefulness in management of vector-borne disease. Some new drugs originate from traditional herb. The best example is qinghao, which has already been developed into new antimalarial drug [14, 15]. At present, Several natural products are proposed for possible usefulness in management of vector-borne diseases (Table 2) [16–19].

## Bioinformatics Databases on Natural Products

At present, there are some bioinformatics databases on natural products that might be useful for searching for natural products in vector-borne disease management. The examples of bioinformatics databases on natural products are presented in Table 3 [20–24].

To derive advantage of database for drug search for vector-borne disease management, the first requirement is a good database construction. A well-constructed database should contain applications of medicinal chemistry, molecular biology and pharmaceutical sciences [25]. Networking strategies should systematize large volumes of genetic and

**Table 3.** Examples of bioinformatics databases on natural products

| Database | Details |
|---|---|
| HERB [20] | HERB is a high-throughput experiment- and reference-guided database of traditional Chinese medicine [20]. |
| TCMSP [21] | TCMSP is a database of systems pharmacology for drug discovery from herbal medicines [21]. |
| NPASS [22] | NPASS is a natural product activity and species source database for natural product research, discovery and tool development [22]. |
| Super Natural II [23] | Super Natural II is a database of natural products [23]. Super Natural II is available at http://bioinformatics.charite.de/supernatural [23]. The database allows a template-based search for similar compounds as well as a search for compound names and specific physical properties [23]. |
| BIOFACQUIM [24] | BIOFACQUIM is a Mexican compound database of natural products [24]. BIOFACQUIM collects profile of physicochemical properties, scaffold content, and diversity, as well as structural diversity based on molecular fingerprints [24]. |

**Table 4.** Steps for using informatics tool for searching for natural products in vector-borne disease management

| Step | Details |
|---|---|
| Looking for candidate | The information and data on candidate might be collated from various resources like ethnobotanical textbooks and literature databases such as PubMed, Science Direct, Wiley, Springer, Tailor and Francis, Scopus, Inflibnet, Google and Google Scholar [17]. |
| Database searching | Database searching for components identification, checking for efficacy and toxicity is done. |
| Bioinformatics clarification | Using bioinformatics tools for structural identification and clarification is done. The studies are on both candidate substance and pathogen of vector borne disease. Structural genomics and proteomics tools play role in this step. |
| Bioinformatucs prediction | Using bioinformatics tools for molecular function, biological process, pathway and possible interaction is done. Ontology and interactomics tools play role in this step. |
| *In vitro* and *in vivo* process | After complete in silico process, the finally recruited candidate will be derived Further studies via standard *in vitro* and *in vivo* pharmacological and clinical studies are performed. |

chemical data and connect genomic information to phenotypic and metabolomic data [26]. When there is a database, searching is the important step for data mining. For data mining, the characteristics of natural products that are routinely searched include biological activity, absorption, distribution, metabolism, excretion, and toxicology [27].

## Steps for Using Informatics Tool for Searching for Natural Products in Vector-Borne Disease Management

There are many important steps for searching for natural products in vector-borne disease management (Table 4). Starting from crude data collection, which usually refers to local traditional and folkway regimens, the standard database search is the first requirement. The database search results can give clues for efficacy and toxicity of the natural product candidate. When there is an evidence of possible efficacy and safety, further molecular clarification is done. Regarding molecular clarification, both structure of natural product candidate and pathogen should be assessed [27]. The structural data will be further used for expressional analysis and interaction analysis. If all in-silico analyses provide that the natural product candidate is good, further *in vitro* and *in vivo* studies will be further performed (Fig. 1, Table 4) [17].

## Example of Bioinformatics Application for Searching for Natural Products in Vector-Borne Disease Management

For better understanding of the process, an example

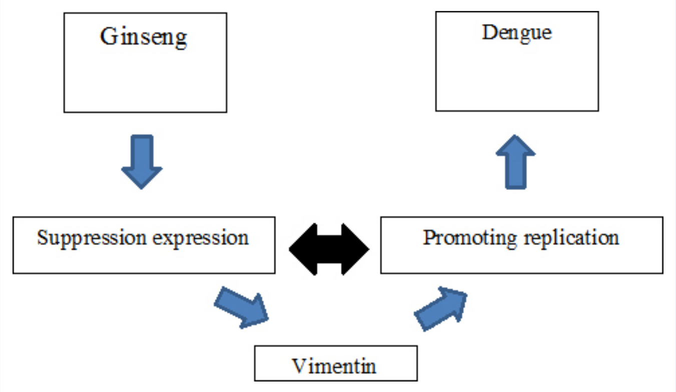

FIGURE 2. Interrelationship network showing the interrelationship between pharmacological process of ginseng and pathophysiological process of dengue at vimentin.

Figure by Wiwanitkit, 2021

of bioinformatics application for searching for natural products in vector-borne disease management is hereby presented. Here, the authors showed an example quoting from a recent report using a network pharmacology analysis to assess the common biological pathway for pharmacological effect of ginseng, a classic Asian herb, and pathophysiological process of dengue, an important tropical mosquito-borne disease [28]. From interrelationship analysis, the author can demonstrate the common pathway via vimentin node. It can show that ginseng can be useful in management of dengue.

This work is a clinical informatics study. The biological process network analysis is done. Based on the concept of network pharmacology [29, 30], the effect of the classical traditional herb in Asia, herb is assessed for its interrelationship with the pathophysiological process of dengue, an important tropical vector-borne infection. The information in biological processes regarding ginseng and dengue is derived from direct database mining using standard international databases, PubMED and SCOPUS.

For interrelationship analysis, the identified biological processes, both pharmacological process of ginseng and pathophysiological process of dengue, are listed and looked for common pathway. The common node is identified and used for construction of the final interrelationship network.

According to the analysis, the author can identify a common node between pharmacological process of ginseng and pathophysiological process of dengue at vimentin. From further interrelationship network analysis, the final interrelationship network is presented in Figure 2.

Using bioinformatics clinical pharmacology network analysis is accepted as an advantage in assessment the effect of traditional herbal regimens [31–33]. The technique is based on informatics analysis starting from pathway searching, identifying of common nodes, rearrangement and final creation of the interrelationship network. This technique is the standard clinical informatics analysis used in previous publications [34, 35]. In this short article, the author performs a preliminary study to test the usefulness of ginseng, a well-known herb, in the management of an important tropical blood infection, dengue.

Based on the present study, it can be shown that there is a common node between pharmacological process of ginseng and pathophysiological process of dengue at vimentin. Ginseng is clarified for its effect on reducing expression of vimentin [35]. Meanwhile, dengue has its important pathological process of using vimentin in replication process [36–38]. It can be concluded that ginseng should have an anti-dengue effect, making it a useful traditional herb for management of dengue.

## Conclusion

Bioinformatics technologies are applicable in new anti-vector-borne disease drug search. Based on genomics, proteomics, chemoinformatics and expressional analysis, new drug candidates can be searched and further tested for expected clinical advantages. Many natural products are the targets for new drug search. Bioinformatics technology can help shorten required searching time for natural products in vector bornedisease management. The data from basic bioinformatics studies leads to further research and development on new anti vector-borne disease drugs.

**Authorship Contributions:** Concept – RM, VW; Design – RM, VW; Supervision – RM, VW; Fundings – RM, VW; Materials – RM, VW; Data collection and/or processing – RM, VW; Analysis and/or interpretation – RM, VW; Literature review – RM, VW; Writing – RM, VW; Critical review – RM, VW.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Use of AI for Writing Assistance:** Not declared.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Peer-review:** Externally peer-reviewed.

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