

ADVANCED REVIEW



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Computational resources in healthcare

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Abstract

Healthcare is the most important component in the life of all human beings as each individual wish to have happy, healthy, and wealthy life-span. Most of the branches of science are dedicated to improve the healthcare. In the era of knowledge mining, informatics is playing a crucial role in different branches of research. Thus, a wide range of informatics-based fields have emerged in the last three decades that include medical informatics, bioinformatics, cheminformatics, pharmacoinformatics, immunoinformatics, and clinical informatics. In the past, a number of reviews have been focused on the application of an informatics-based field in the healthcare. In this review, an attempt is made to summarize the major computational resources developed in any informatics-based field that have an application in healthcare. This review enlists computational resources in following groups - drug discovery, toxicity prediction, vaccine designing, disease biomarkers, and Internet of Things. We mainly focused on freely available, functional resources like data repositories, prediction models, standalone software, mobile apps, and web services. In order to provide service to the community, we developed a health portal that maintain links related to healthcare <http://webs.iiitd.edu.in/>.

This article is categorized under:

Application Areas > Health Care

KEYWORDS

bioinformatics, cheminformatics, clinical informatics, health informatics, pharmacoinformatics

1 | INTRODUCTION

Healthcare is a multifaceted system established with the primary purpose of prevention, diagnosis and treating human health-related diseases (Dash et al., 2019; Imhoff et al., 2001). In last three decades, number of informatics-based fields have been developed to facilitate healthcare. It includes cheminformatics, pharmacoinformatics, health informatics, and medical/clinical informatics (Herland et al., 2014). The evolving field of informatics in healthcare is generating vast wealth of biological and clinical data (Abul-Husn & Kenny, 2019). For instance, open-source electronic health record systems have gained importance which provide accurate, latest, and complete information about patients at the point of care. Due to advances in sequencing technology, growth of biological data is

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exponential in last two decades (Manzoni et al., 2018). The growth of the data is in almost all fields, for example, genomics, proteomics, structural information, biomedical images, disease pathways, and electronic health records (Abul-Husn & Kenny, 2019; Li et al., 2013). Bioinformatics plays a prominent role in compiling, storing, annotating and analyzing such kind of data and further make it accessible to every biologist and non-biologist. In the past, there have been many reviews explaining the role of bioinformatics in healthcare (Branco & Choupina, 2021; Kuznetsov et al., 2013; Majhi et al., 2019; Singla et al., 2013a).

The global healthcare burden is significantly rising due to increase in novel infectious diseases (Bloom & Cadarette, 2019). There is a dire need for efficient drugs to treat these deadly diseases, which enhances the demand for drug discovery and development. However, the drug development process has become alarmingly costly and time consuming and is one of the important aspects of healthcare (Rosales-Hernandez & Correa-Basurto, 2015). Recent advances in informatics-based fields such as cheminformatics and pharmacoinformatics have increased the efficiency of drug discovery process by bringing down the cost and time before preclinical and clinical trials (Engel, 2006; Hughes et al., 2011). Various software, tools, and methods have been developed to study drug target identification, lead compound selection, identifying ligand binding pockets, screening the drug candidates, and in silico ADMET property prediction for drug discovery process (Jamkhande et al., 2017). Several findings have been reported in the literature that support the contribution of cheminformatics and pharmacoinformatics in healthcare (Ou-Yang et al., 2012; Strzelecki et al., 2013).

In addition to drug discovery, vaccine development and immunoinformatics have resulted in a remarkable improvement in global health (Oli et al., 2020). The use of vaccines has successfully controlled various contagious diseases including COVID-19, polio, and smallpox (Forni et al., 2021; Greenwood, 2014). The traditional approach for vaccine development is a tedious process that involves administering the whole pathogen after attenuation (Pollard & Bijker, 2021). To overcome the shortcomings, immunoinformatics paved the way for better understanding of vaccine development (Kardani et al., 2020). Computational immunology tools and databases make it easier and enhance the possibility to discover potential vaccine candidates (Dhanda et al., 2017; Usmani et al., 2018b).

Another growing area in informatics is medical/clinical informatics, where it deals with the management of patient data, clinical knowledge and other information related to patient care (Wyatt & Liu, 2002). It includes the well curated databases, tools and methods for the identification of disease biomarkers, which aids in disease diagnosis (Coskun & Ozcan, 2014). Beside this, Internet of Things (IoTs) is the emerging field which has completely transformed the healthcare industry by bringing patients, doctors, and hospitals together (Pradhan et al., 2021). The well-known IoT applications in today scenario are mobile apps, telemedicine, and sensor-based wearable devices (Savage, 2020; Tornador et al., 2019).

In this review, we have focused on summarizing the various computational resources used in the healthcare sector. In the recent years, healthcare sector became more digitalized and advanced. Here, we have made an attempt to compile the freeware and open-source computational tools, methods and databases that are commonly used in various informatics-based fields. The objective of this review is to provide an exhaustive view about the advancements in the area of healthcare, comprising, drug discovery, toxicity and its adverse effects, vaccine development, disease biomarkers, and healthcare IoTs as shown in Figure 1. For better understanding of the area, these tools are categorized as databases, web servers, standalone, and mobile apps developed in the respective areas.

This review article outlines the computational resources developed in different areas of healthcare and health-informatics. First, we summarized the major tools and databases developed in the field of drug discovery. We mainly focused on tools commonly used for designing peptide-based and small-chemical based drug discovery. Second, we have compiled the existing computational repositories and tools for addressing the toxicity of the molecules and its side effects. Third, we underscored resources heavily used for vaccine development and methods for predicting peptides that can activate different arms of immune system. Thereafter, we have compiled several important well-known repositories and prediction tools for biomarker discovery. Finally, we have discussed briefly about the IoTs in healthcare sector. The huge amount of data generated by healthcare-specific IoT products opens up enormous opportunities and hold the potential to transform healthcare. The tools and repositories are organized in the tabular form. The tables depict the name of the tool, with brief description and link, its type (database, standalone, webserver, and mobile app) and its references. We have concluded the review by explaining the utility of the tools and database in the different areas of healthcare.

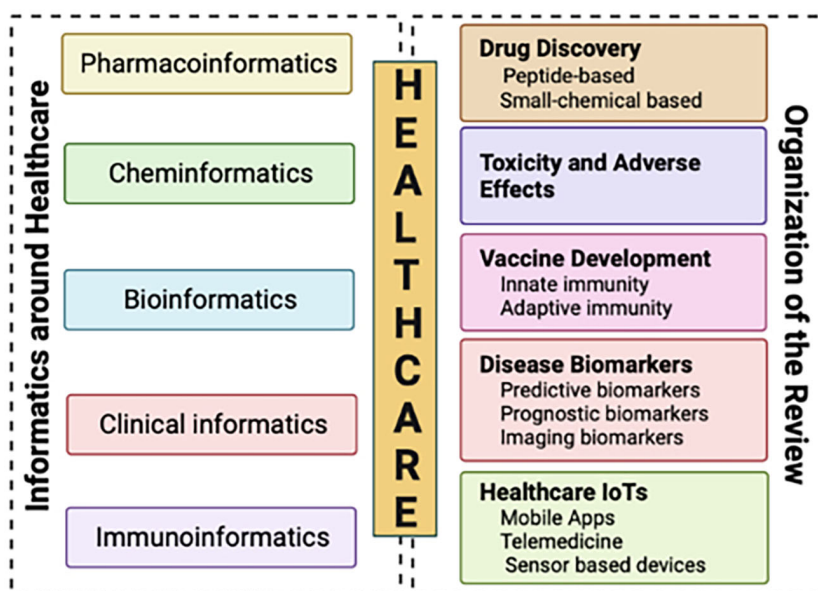


FIGURE 1 The complete architecture of the review

2 | DRUG DISCOVERY

Drugs are chemicals/molecules, which are used for the treatment, curation, and prevention of life-threatening diseases. There is a need to discover/design new drugs that are effective against existing and emerging diseases (Kumar, 2013). Drug discovery is a time-consuming as well as costly affair, an average discovery of a drug takes around 10–15 years and expenditure of billions of dollars (Jamkhande et al., 2017). In order to facilitate drug discovery, number of computational resources have been developed over the years (Hodos et al., 2016; Kuhlmann, 1997). Drugs may be based on wide range of molecules that include small chemicals, carbohydrates, lipids, polysaccharides, peptides, and proteins. In this review, we have only summarized computational resources developed for protein and small chemicals-based drugs. Traditionally, most of drugs are based on small chemicals, recently protein/peptide-based drugs have emerged as an alternate to chemical-based drugs. These peptide-based drugs have number of advantages over chemical-based drugs that includes highly versatile, high specificity, and low toxicity (Usmani et al., 2017). For instance, Imcivree (Setmelanotide) and Hepcludex are the peptide-based drugs which are approved and used to treat obesity and Hepatitis D virus infection, respectively. In Table 1, we have enlisted the tools, web servers and databases used for peptide-based drug discovery. Similarly, we summarized major resources commonly used for designing small chemical-based drug discovery in Table 2.

3 | TOXICITY AND ADVERSE EFFECTS

Toxicity is defined as adverse effects shown by any substance, drug or vaccine on any organism. The toxic effects can range from minor reactions to life-threatening consequences to the health of the patient. Pharmaceutical companies working in the area of healthcare need to do safety assessments during the drug discovery process. In order to reduce the toxicity and produce a better clinical drug candidate, several tools and repositories have been developed (Di, 2016). For instance, to estimate the toxicity of the molecules, tools like Toxtree (Patlewicz et al., 2008), ProTox-II (Banerjee et al., 2018), and many other tools exist. Apart from the prediction tools, various databases are also available, storing the information for the molecules that can cause toxicity, such as Comparative Toxicogenomics Database (Davis et al., 2017), and Distributed Structure Searchable Toxicity (Grulke et al., 2019) which contains more than 200,000 chemical data collected from different sources. Table 3 enlists the tools and databases used for toxicity prediction and adverse effects.

TABLE 1 List of major computational tools and databases available for designing and discovering peptide-based drugs

Tool	Description (link)	Type (D/S/W/M)	References
AniAMPpred	Prediction of antimicrobial peptides in animal kingdom (https://aniamppred.anvil.app/)	W	Sharma et al. (2021a)
B3Pdb	Compilation of blood–brain barrier penetrating peptides (https://webs.iiitd.edu.in/raghava/b3pdb/)	D/W	Kumar et al. (2021)
B3Pred	Blood–brain barrier penetrating peptides prediction (https://webs.iiitd.edu.in/raghava/b3pred/)	W/S	Vinod Kumar et al. (2021)
AlgPred 2.0	Highly accurate method for predicting allergic proteins (https://webs.iiitd.edu.in/raghava/algpred2/)	W/S	Sharma et al. (2020)
AntiCP 2.0	Improved method for identification of anticancer peptides (https://webs.iiitd.edu.in/raghava/anticp2/)	W/S	Agrawal et al. (2020)
HemoPI-MOD	Hemolytic potency of chemically modified peptides (https://webs.iiitd.edu.in/raghava/hemopimod/)	W/S	Kumar et al. (2020b)
Antifp	Prediction of antifungal peptides (https://webs.iiitd.edu.in/raghava/antifp/)	W/S/M	Agrawal et al. (2018)
AntiMPmod	Antimicrobial potential of chemically modified peptides (https://webs.iiitd.edu.in/raghava/antimpmod/)	W	Agrawal and Raghava (2018)
AntiTbPred	Prediction of antitubercular peptides (https://webs.iiitd.edu.in/raghava/antitbpred/)	W	Usmani et al. (2018a)
CellPPD-MOD	Computation of chemically modified cell penetrating peptides (https://webs.iiitd.edu.in/raghava/cellppdmod/)	W	Kumar et al. (2018)
PlifePred	Estimation of half-life of peptides in blood (https://webs.iiitd.edu.in/raghava/plifepred/)	W	Mathur et al. (2018b)
TopicalPdb	Repository of topically delivered peptides (https://webs.iiitd.edu.in/raghava/topicalpdb/)	D/W	Mathur et al. (2018a)
THPdb	Compilation of peptide/protein based therapeutic molecules (https://webs.iiitd.edu.in/raghava/thpdb/)	D/W	Usmani et al. (2017)
CPPSite2	Database of cell-penetrating peptides (https://webs.iiitd.edu.in/raghava/cppsitere/)	D/W	Agrawal et al. (2016)
AHTpin	Designing antihypertensive peptides (https://webs.iiitd.edu.in/raghava/ahtpin/)	W	Kumar et al. (2015)
AntiAngioPred	Prediction of anti-angiogenic peptides (http://clri.res.in/subramanian/tools/antiangiopred/)	W	Ettayapuram Ramaprasad et al. (2015)
CancerPPD	Database of anticancer peptides and proteins (https://webs.iiitd.edu.in/raghava/cancerppd/)	D/W/M	Tyagi et al. (2015)
TumorHPD	Designing tumor homing peptides (https://webs.iiitd.edu.in/raghava/tumorhpd/)	W	Sharma et al. (2013)
AntiBP2	Webserver for antibacterial peptide prediction (https://webs.iiitd.edu.in/raghava/antibp2/)	W	Lata et al. (2010)

Abbreviations: D, database; M, mobile apps; S, standalone; W, webserver.

4 | VACCINE DEVELOPMENT

The vaccine is a biological composition that can provoke an immune response and provides active acquired immunity against any infection or disease. In order to induce an immune response, it must contain antigens that resemble the disease-causing pathogen in its weakened or killed form, its toxins, or one of its surface proteins to confer protection on subsequent exposure to that pathogen (Pollard & Bijker, 2021). The conventional method for designing a vaccine is a time-consuming and tedious process, which involves administering the whole pathogen after its attenuation. The administration

TABLE 2 List of tools and databases for small chemical-based drug discovery

Tool	Description (link)	Type (D/S/W/M)	References
<i>Resources for chemical compounds</i>			
PubChem	Database of bioassays, compounds, and substances (https://pubchem.ncbi.nlm.nih.gov/)	D/W	Kim et al. (2021)
ChEMBL	Database of drug like molecules (https://www.ebi.ac.uk/chembl/db)	D/W	Gaulton et al. (2012)
Zinc15	Database of commercially available compounds for virtual screening (http://zinc.docking.org/)	D	Sterling and Irwin (2015)
DrugBank 5.0	Comprehensive information about drugs (https://go.drugbank.com/)	D/W	Wishart et al. (2018)
BindingDB	Binding affinity of PDB ligands (http://www.bindingdb.org/)	D/W	Liu et al. (2007)
SuperDRUG2	Database of approved/marketed drugs (http://cheminfo.charite.de/superdrug2/)	D/W	Siramshetty et al. (2018)
<i>Molecular descriptors</i>			
PaDEL	1D, 2D, 3D, and fingerprints calculation (http://padel.nus.edu.sg/software/padeldescriptor)	S	Yap (2011)
CDK	Chemistry Development Kit (http://cdk.sourceforge.net)	S	Steinbeck et al. (2003)
Mordred	Molecular descriptor calculator (https://github.com/mordred-descriptor/mordred)	W/S	Moriwaki et al. (2018)
<i>Docking software</i>			
Dock 6	Standalone software for molecular docking (http://dock.compbio.ucsf.edu/)	S	Allen et al. (2015)
AutoDock Vina	Program for molecular docking and virtual screening (http://vina.scripps.edu/)	S	Trott and Olson (2010)
Autodock	Molecular modeling simulation software (http://autodock.scripps.edu/)	S	Morris et al. (2008)
<i>QSAR model generation</i>			
QSAR-Co	Classification-based QSAR model development (https://sites.google.com/view/qsar-co)	S	Ambure et al. (2019)
D PubChem	Web tool for QSAR modeling and high-throughput virtual screening (https://www.cbrc.kaust.edu.sa/dpubchem/)	W	Soufan et al. (2018)
Weka	Collection of machine learning algorithm for the development of QSAR based models (https://www.cs.waikato.ac.nz/~ml/weka/)	S	Frank et al. (2004)
<i>Structure optimization</i>			
TINKER	Software tools for molecular design (http://dasher.wustl.edu/tinker/)	S	Rackers et al. (2018)
Frog	Generation of free online drug conformation (http://bioserv.rpbs.jussieu.fr/cgi-bin/Frog)	W	Leite et al. (2007)
Openbabel	The open source chemistry toolbox (http://openbabel.org/)	S	O'Boyle et al. (2011)
<i>Drug target inhibitors</i>			
EGFRpred	QSAR based model for predicting EGFR inhibitors (https://webs.iitd.edu.in/oscadd/egfrpred/)	W/S	Singh et al. (2015)
MDRIpred	Prediction of inhibitor against drug tolerant <i>Mycobacterium tuberculosis</i> (https://webs.iitd.edu.in/oscadd/mdri/)	W	Singla et al. (2013b)
GDoQ	Prediction of inhibitors against Mycobacterial GlmU (https://webs.iitd.edu.in/raghava/gdoq/)	W	Singla et al. (2011)

Abbreviations: D, database; M, mobile apps; S, standalone; W, webserver.

of the whole pathogen increases the toxicity issues caused by the unwanted biomaterial of the pathogen, hence posing safety threats. In the past, studies have shown that small regions of the pathogen, such as a small peptide, can stimulate the different arms of the immune system (Chaplin, 2010). Thus, a small peptide can also be used as a potential vaccine

TABLE 3 List of computational tools and databases commonly used for predicting toxicity of molecules and macromolecules

Tool	Description (link)	Type (D/S/W/M)	References
admetSAR 2.0	Tool to predict the chemical ADMET properties (http://lmmd.ecust.edu.cn/admet2/)	W	Yang et al. (2019a)
ADMETopt	Optimization of lead compounds and ADMET screening (http://lmmd.ecust.edu.cn/admet2/admetopt/)	W	Yang et al. (2018)
ADMETlab	Web-service for systematic ADMET evaluation of chemicals (http://admet.scbdd.com/)	W	Dong et al. (2018)
DrugMint	Computation of drug-like molecules (https://webs.iiitd.edu.in/oscadd/drugmint/)	W/S	Dhanda et al. (2013b)
MetaPred	Prediction of drug metabolizing CYP450 isoforms (https://webs.iiitd.edu.in/raghava/metapred/)	W/S	Mishra et al. (2010)
SwissADME	Tool to assess pharmacokinetics, drug-likeness and related parameters of small molecules (http://www.swissadme.ch)	W	Daina et al. (2017)
vNN	Webserver for ADMET predictions (https://vnnadmet.bhsai.org/)	W	Schyman et al. (2017)
ADVERpred	Web-service for prediction of adverse effects of drugs (http://www.way2drug.com/adverpred/)	W	Ivanov et al. (2018)
BTXpred	Prediction of bacterial toxins (https://webs.iiitd.edu.in/raghava/btxpred/)	W	Saha and Raghava (2007a)
ChAIPred	Computation of allergenicity of chemical compounds (https://webs.iiitd.edu.in/raghava/chalpred/)	W	Sharma et al. (2021)
CTD	The comparative toxicogenomics database (http://ctdbase.org/)	D/W	Davis et al. (2017)
eToxPred	Calculate toxicity and synthetic accessibility of compounds (https://github.com/pulimeng/etoxpred/)	S	Pu et al. (2019)
NTXpred	Webserver for predicting neurotoxins (https://webs.iiitd.edu.in/raghava/ntxpred/)	W	Saha and Raghava (2007b)
Pred-hERG	Computational tool for predicting cardiac toxicity (http://labmol.farmacia.ufg.br/predherg/)	W	Braga et al. (2015)
Pred-Skin	Web portal for accurate prediction of human skin sensitizers (http://labmol.com.br/predskin/)	W/M	Braga et al. (2017)
ProTox-II	Prediction of toxicity of chemicals (http://tox.charite.de/protox_II)	W	Banerjee et al. (2018)
SIDER 4.1	Database on marketed medicines and their adverse drug reactions (http://sideeffects.embl.de/)	D/W	Kuhn et al. (2016)
ToxiPred	Prediction of aqueous toxicity of small chemical molecules (https://webs.iiitd.edu.in/raghava/toxipred/)	W/S	Mishra et al. (2014)
ToxinPred	Estimating toxicity of proteins (https://webs.iiitd.edu.in/raghava/toxinpred/)	S/W	Gupta et al. (2013b)

Abbreviations: D, database; M, mobile apps; S, standalone; W, webserver.

candidate. However, the major challenge is the identification of the small peptides (epitopes or antigenic regions) that can be utilized for immunization against disease-causing pathogens. Several computational tools have been developed to identify the antigenic regions or epitopes of the pathogenic organism (Dhanda et al., 2017; Oli et al., 2020; Pollard & Bijker, 2021). In this study, we have compiled various epitope-based vaccine prediction tools and repositories (Table 4).

5 | DISEASE BIOMARKERS

Identification of disease, disease progression and level of severity are major challenges in the field of healthcare, which involve discovery of appropriate disease biomarkers (FDA-NIH Biomarker Working Group, 2016). Biomarkers

TABLE 4 List of resources developed for predicting peptide that can activate different arms of immune system

Tool	Description (link)	Type (D/S/W/M)	References
<i>Adaptive immunity</i>			
pVACtools	Computational toolkit to identify cancer neoantigens (https://pvactools.readthedocs.io/)	W/S	Hundal et al. (2020)
IL-6pred	Prediction of interleukin-6 inducing peptides (https://webs.iiitd.edu.in/raghava/il6pred/)	W/S	Dhall et al. (2021)
IEDB	Database of immune epitopes and analysis resources (http://www.iedb.org/)	D/W	Vita et al. (2019)
NetMHCIIpan 3.2	Webserver predicts binding of peptides to MHC class II molecules (http://www.cbs.dtu.dk/services/NetMHCIIpan-3.2/)	W	Jensen et al. (2018)
NetMHCpan 4.0	Prediction of peptide–MHC class I binding using artificial neural networks (http://www.cbs.dtu.dk/services/NetMHCpan-4.0/)	W	Jurtz et al. (2017)
IL-10pred	Identification of interleukin-10 inducing peptides (https://webs.iiitd.edu.in/raghava/il10pred/)	W	Nagpal et al. (2017b)
IL4pred	Prediction of interleukin-4 inducing peptides (https://webs.iiitd.edu.in/raghava/il4pred/)	W/S	Dhanda et al. (2013a)
IFNepitope	Designing and scanning interferon-gamma inducing epitopes (https://webs.iiitd.edu.in/raghava/ifnepitope/)	W/S	Dhanda et al. (2013c)
LBtope	Improved method for predicting linear B-cell epitopes (https://webs.iiitd.edu.in/raghava/lbtope/)	W/S	Singh et al. (2013)
IgPred	B-cell epitopes for induce different class of antibodies (https://webs.iiitd.edu.in/raghava/igpred/)	W/S	Gupta et al. (2013a)
DiscoTope 2.0	Prediction of discontinuous B cell epitopes in a protein structure (http://www.cbs.dtu.dk/services/DiscoTope/)	W	Kringelum et al. (2012)
Cbtope	Prediction of conformational B-cell epitope (https://webs.iiitd.edu.in/raghava/cbtope/)	W/S	Ansari and Raghava (2010)
ABCpred	ANN based method for predicting B cell epitopes (https://webs.iiitd.edu.in/raghava/abcpred/)	W/S	Saha and Raghava (2006)
Pcleavage	Identification of proteasomal cleavage sites in a protein (https://webs.iiitd.edu.in/raghava/pcleavage/)	W/S	Bhasin and Raghava (2005)
CTLPred	A direct method for prediction of CTL epitopes (https://webs.iiitd.edu.in/raghava/ctlpred/)	W/S	Bhasin and Raghava (2004b)
TAPPred	Prediction of TAP binding peptides (https://webs.iiitd.edu.in/raghava/tappred/)	W	Bhasin and Raghava (2004a)
ProPred1	Computing promiscuous MHC class-I binding sites (https://webs.iiitd.edu.in/raghava/propred1/)	W/S	Singh and Raghava (2003)
ProPred	Prediction of promiscuous MHC class-II binding sites (https://webs.iiitd.edu.in/raghava/propred/)	W/S	Singh and Raghava (2001)
<i>Innate immunity and predicted vaccine candidate</i>			
PRRpred	Prediction of pattern-recognition receptors (https://webs.iiitd.edu.in/raghava/prrpred/)	W	Kaur et al. (2020a)
PRRDB 2.0	An archive of pattern-recognition receptors and their ligands (https://webs.iiitd.edu.in/raghava/prrdb2/)	D/W	Kaur et al. (2019a)
VaxinPAD	Designing peptide-based vaccine adjuvants (https://webs.iiitd.edu.in/raghava/vaxinpad/)	W	Nagpal et al. (2018)
VLCvirus	Subunit vaccine candidates against lung cancer associated viruses (https://webs.iiitd.edu.in/raghava/vlcvirus/)	D/W	Lathwal et al. (2021)

(Continues)

TABLE 4 (Continued)

Tool	Description (link)	Type (D/S/W/M)	References
CoronaVIR	Web resource for designing vaccine candidate against COVID19 (https://webs.iiitd.edu.in/raghava/coronavir/)	W	Patiyal et al. (2020)
Cancertope	Designing genome-based personalized cancer immunotherapy (https://webs.iiitd.edu.in/raghava/cancertope/)	W	S. Gupta, (2016)
EbolaVCR	Web resource for designing therapeutics against Ebola virus (https://webs.iiitd.edu.in/oscadd/ebola/)	W	Dhanda et al. (2016a)

Abbreviations: D, database; M, mobile apps; S, standalone; W, webserver.

have been divided into various subtypes based on their applications, for instance, diagnostic biomarkers are used for the detection of cancer at an early stage (Kim & Hong, 2021). A predictive biomarker is used to identify the patients that likely benefit from specific therapeutic approaches (Sechidis et al., 2018). Predictive biomarkers, such as estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2, are well-known markers for breast cancer (Oldenhuis et al., 2008). On the other hand, a prognostic biomarker is a clinical or biological characteristic that can give valuable information on the patient health outcome (Sechidis et al., 2018). Apolipoprotein A1, is a strong marker for cardiovascular diseases (Florvall et al., 2006). Digital biomarkers refer to the data which are gathered and measured by digital devices. For example, LIFEx is a user-friendly software which is used to extract different radiomic features illustrating tumor heterogeneity (Nioche et al., 2018). Thus, a variety of several bioinformatics tools/webserver for biomarkers identification have been developed due to rise in several biological data. We have highlighted the recent tools and databases and their potential in diagnostic, prognostic, and predictive applications in Table 5.

6 | HEALTHCARE IoTs

It is not practically feasible for medical practitioners to monitor health conditions of their patients regularly. There is a need to develop alternate techniques to aid doctors in monitoring wide range of clinical parameters 24×7 of their patients. IoT is one of the alternatives, which completely transformed the healthcare industry (Pradhan et al., 2021). It is bringing myriad benefits to the patients, families, physicians, hospitals and insurance companies. The term IoT was coined for the first time in 1999 by Kevin Ashton during his work at Procter & Gamble (Alansari et al., 2018; Kramp et al., 2013). It refers to a network of connected medical devices that can generate, collect, and store data as well as allow to analyze, and transmit data (Patra et al., 2021). It helps in modeling the spread of disease and to control disease outbreaks (Dash et al., 2019). IoT healthcare services are mainly composed of three components such as publisher, message broker, and subscriber (Oryema et al., 2017). The publisher represents a network of connected sensors or hand-held devices that records and send the patients' vital information. This information includes blood pressure, heart rate, temperature, oxygen saturation, electrocardiogram, and electromyography. The broker will process and store the data on the cloud. Ultimately, the subscriber will monitor the patient's data, which can be accessed and viewed via a smartphone, computer, tablet, or other devices (Dang et al., 2019). IoT-based healthcare systems revolutionized the healthcare facilities and management. Some of the practical examples of the IoTs are wearable devices, ambient (non-wearable) devices, mobile-health applications (m-Health apps), and electronic health records (EHR) (Jayaraman et al., 2019). Several wearable IoT devices are available in the market such as wristband sensors (Fitbit, Philips sensor DTI-2) (Kikhia et al., 2016), smart watches (Apple watch, Samsung gear), and health monitors (Electrocardiogram, Heart rate, Glucose monitor). Flexible and fabric sensors that can be attached to skin include Zio Patch from iRhythm (used to monitor the cardiac rhythm) (iRhythm, 2018) and sense A/S (used for continuous blood pressure monitoring) (SenseA/S, 2018). Ambient (non-wearable) IoT devices includes motion sensors, sound sensors, bed sensors which are heavily used by elderly people suffering from dementia, Parkinson's disease to keep track of their daily activities.

TABLE 5 List of computational resources for identification of biomarkers for detecting wide range of diseases

Tool	Description (link)	Type (D/S/W/M)	References
<i>Predictive biomarkers</i>			
CancerCSP	Classification of early and late stages of clear cell renal cell carcinoma (https://webs.iiitd.edu.in/raghava/cancercsp/)	W	Bhalla et al. (2017)
CancerEnD	Database of cancer associated enhancers (https://webs.iiitd.edu.in/raghava/cancerend/)	D/W	Kumar et al. (2020a)
CancerLiver	Repository of liver cancer-specific biomarkers (https://webs.iiitd.edu.in/raghava/cancerliver/)	D/W	Kaur et al. (2020b)
CancerLSP	Identification of early stage liver hepatocellular carcinoma patients (http://webs.iiitd.edu.in/raghava/cancerlsp/)	W	H. Kaur,- (2019)
CancerTSP	Discrimination of early and late-stage samples of thyroid carcinoma (http://webs.iiitd.edu.in/raghava/cancertsp/)	W	Bhalla et al. (2020)
CRC-EBD	Database for epigenetic biomarkers on colorectal cancer (http://www.sysbio.org.cn/EBD/)	D/W	Liu et al. (2020)
MarkerDB	Database of molecular biomarkers (https://markerdb.ca/)	D/W	Wishart et al. (2021)
PTSDDB	Database for post-traumatic stress disorder biomarkers (https://ptsd.scai.fraunhofer.de/)	W	Domingo-Fernandez et al. (2019)
<i>Prognostic biomarkers</i>			
CMcrpred	Estimate survival risk in cutaneous melanoma patients (https://webs.iiitd.edu.in/raghava/cmcrpred/)	W	Arora et al. (2020)
CRCRpred	Prediction of risk scores of colorectal cancer patients (https://webs.iiitd.edu.in/raghava/crcrpred/)	W	Lathwal et al. (2019)
SKCMhrp	Classification of high-risk cutaneous melanoma patients (https://webs.iiitd.edu.in/raghava/skcmhrp/)	W	Dhall et al. (2020)
SurvExpres	Tool and database for cancer gene expression data using survival analysis (http://bioinformatica.mty.itesm.mx/SurvExpress)	D/W	Aguirre-Gamboa et al. (2013)
<i>Imaging biomarkers</i>			
ePAD	Tool to calculate quantitative imaging biomarkers of cancer treatment response (http://epad.stanford.edu/)	S	Rubin et al. (2019)
LIFEx	Freeware to extract radiomic features (https://www.lifexsoft.org/)	S	Nioche et al. (2018)
TCIA	Webserver to create an easily accessible archive of cancer images (https://www.cancerimagingarchive.net/)	W	Clark et al. (2013)
3D Slicer	Medical image computing (https://www.slicer.org/)	W	Fedorov et al. (2012)

Abbreviations: D, database; M, mobile apps; S, standalone; W, webserver.

Mobile-health applications are smartphones based health apps that have potentially improved the healthcare system. This digital health technology has made possible to manage self-health. For example, Aarogya Setu (developed by the Government of India) helps to get the data related to COVID-19 patients. Similarly, Babylon health is all-in-one healthcare on phone to check symptoms and offers appropriate medical advice (Babylon, 2018). Chatbot apps aids the patients' to connect with physicians for their treatment, such as, IBM chatbot. It is an artificial intelligence based app that provides personal assistance and advice the patients' suffering from arthritis (IBM Press Release, 2017). A voice-based technology named Sonde, utilizes voice tones to determine the physical and mental health conditions such as, COVID-19, asthma, and anxiety. Another IoTs, EHR are the digital version of the patients' health records in the form of magnetic resonance imaging and X-ray, ultrasound images. Table 6 overviews the various mobile health apps, webserver and sensor devices available for IoT-based healthcare system.

TABLE 6 List of m-health apps, telemedicine, and different types of IoT-based devices

Tool	Description (link)	References
1mg	An online pharmacy with a wide range of prescription (https://www.1mg.com/)	
Aarogya Setu	A mobile app developed to fight against coronavirus infection in India (https://play.google.com/store/apps/details?id=nic.goi.aarogyasetu&hl=en_IN&gl=US)	
AIIMS-WHO CC ENBC	App for nursing colleagues and neonatologist across small hospitals (https://play.google.com/store/apps/details?id=drdeorari.aiims.enc&hl=en_IN&gl=US)	
Babylon health	All-in-one healthcare on phone to check symptoms and get medical advice (https://www.babylonhealth.com/)	
CoDysAn	A telemedicine tool for patients with congenital dyserythropoietic anemia (http://www.codysan.eu/)	Tornador et al. (2019)
Comarch Healthcare	Provides a wide range of healthcare solutions (https://www.comarch.com/healthcare/)	
eSanjeevaniOPD	A teleconsultation service to provide healthcare services at homes (https://esanjeevaniopd.in/)	
Lybrate	Consult doctors online (https://www.lybrate.com/)	
ManageMyHealth	Comprehensive telemedicine solution (https://www.managemyhealth.co.nz/m/)	
National Health Portal India	A single point access for authenticated health information (https://www.india.gov.in)	

Abbreviations: D, database; M, mobile apps; S, standalone; W, webserver.

7 | CASE STUDY

Computational resources can be used to discover several biomolecules in a short span of time with limited cost. One such example is the application of a synergistic approach (in-silico and experimental) for the discovery of novel and efficient cell-penetrating peptides (CPPs) in our research group. Initially, our group had developed a repository named CPPsite (Gautam et al., 2012) for compiling CPPs from literature. These peptides have been used for developing a method CellPPD (Gautam et al., 2013) for predicting and designing CPPs. In order to obtain the best CPPs, all proteins in Swiss-Prot have been scanned using CellPPD. The top CPPs predicted by CellPPD have been synthesized and evaluated in vitro using cancer cell lines (Gautam et al., 2015). Among the top CPPs, one peptide named IMT-P8 (IMT-P8; Institute of Microbial Technology-Peptide 8) had been identified to be more efficient than TAT peptide. In another study, we have demonstrated that the predicted peptide has the ability to penetrate the mouse skin tissue and deliver a drug molecule (Gautam et al., 2016). In addition to this, we have also showed that the CPP-antibiotic combination therapy could fight against methicillin-resistant *Staphylococcus aureus* (MRSA) infections. To support these findings, the study has been patented (Raghava & Gautam, 2018). This promising discovery enhanced the utility of the computational resources developed in the past to identify new CPP sequences.

8 | CONCLUSION AND FUTURE ASPECTS

The expansion in diverse informatics-based fields has resulted in vast amounts of biological and clinical data in the healthcare sector. This massive amount of data can be used to identify drug/vaccine targets that aids in designing medicine to cure diseases. These informatics-based fields have led to the development of various computational tools, databases, and web services for wide range of health-associated applications. Informatics-based fields like health informatics, bioinformatics, cheminformatics, pharmacoinformatics, immunoinformatics, and clinical informatics have not only reduced the time for experimental studies but also leads to the identification and design of novel vaccine candidates and disease biomarkers. After the extensive study on the different areas of healthcare, we noticed that there is a limited number of open-source software/tools for scientific and academic purposes compared with commercial tools. For instance, there are a few tools available to predict the property of chemically modified peptides. There is also fewer open-source docking software for the drug discovery process are available. Hence, this can be the potential future scope

to develop more accurate and open-source tools in this field. We anticipate that this review will be beneficial to the research community working in the healthcare sector.

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CONFLICT OF INTEREST

The authors have declared no conflicts of interest for this article.

AUTHOR CONTRIBUTIONS

Neelam Sharma: Conceptualization (equal); data curation (equal); methodology (equal); resources (equal); writing – original draft (equal); writing – review and editing (equal). **Leimarembi Devi Naorem:** Conceptualization (equal); data curation (equal); methodology (equal); resources (equal); writing – original draft (equal); writing – review and editing (equal). **Satakshi Gupta:** Data curation (equal); resources (equal). **Gajendra P.S. Raghava:** Conceptualization (lead); data curation (lead); methodology (lead); resources (equal); supervision (lead); writing – original draft (equal); writing – review and editing (lead).

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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