Optimization of Drug Design Composition by Hybrid Islamic and Evolutionary Medicine for Covid-19 and Its New Variants Using Geometric Time Variants Extreme Genetic Algorithm

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Abstract. There is a difficulty in building the implementation of a computational model to build a complex Covid-19 drug design involving a smart ecosystem. Covid-19 and the drug design of its new variants are formed by combining the appropriate compound and dose as an antiviral. Drug designs as the candidates for Covid-19 drugs can be in the form of herbal medicines and other materials. In computing the design of this drug, the encountered problem is the way to separate the features between the mixed compounds. The feature extraction received will be optimized into compounds that are useful as Covid-19 drug candidates. On the other hand, drug design using manual computational methods is very complicated and requires a fairly long-time estimation in forming the proper compound with many variants of each compound. From the problems that occur, it requires a system that can perform drug design computations quickly and precisely. Therefore, a new method of combining extreme learning machines and genetic algorithms is made called Geometric Time Variants (GTV) Extreme Genetic Algorithm (XtremeGA or eXGA or ExGA). As a result, drug design optimization using historical data by hybrid Islamic and evolutionary medicine for Covid-19 and its new variants can work quickly, optimally, and achieved convergence conditions.

Keywords: Hybrid Islamic and Evolutionary Medicine · Covid-19 and It's New Variants · Geometric Time Variants · Extreme Genetic Algorithm · meta-Deep AI Medicine Engine

1 Introduction

Coronavirus disease (Covid-19) is the name of the latest novel coronavirus variant which was first discovered in the city of Wuhan, China. This virus has a very fast spread from the first case announced by the World Health Organization (WHO) at the end of 2019

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[1]. At the beginning of the spread of this virus, WHO included it in an epidemic status, but because the spread of the corona virus was very fast, WHO made the Covid-19 case a pandemic. The spread of this virus is very fast and very difficult to control. To date, there is no effective drug or vaccine that has been found to cure this virus [2]. To overcome the spread of the covid-19 virus, especially this new variant, it requires a support from various parties, such as the community in complying with health protocols, government agencies, health experts who develop drugs for the corona virus, and IT experts to help find drug formulations and appropriate extraction by doing model learning and optimization [3]. In the field of informatics and technology, development and determination of covid-19 drugs can be carried out by applying machine learning and optimization methods [4–8].

Related research that has been carried out is to create a classification system for the efficacy of herbal medicine on the basis of the plant ingredients contained in it by using the support vector machine (SVM) method and implementing k-means clustering to perform feature selection and using variance to evaluate the results of clustering with the data consisting of 3138 types of herbal medicine and 465 types of plants. Then, the results of the clustering succeeded in reducing the amount of data to 3047 types of herbs with 236 types of plants. The results of the classification using SVM combined with the clustering using K-Means resulted in an accuracy of 71.5% [9]. The next research is a multidisciplinary team study from UI and IPB related to pharmacophore mapping, molecular anchoring for the determination of compounds in anti-Covid-19 drug candidates from natural ingredients in Indonesia by Big Data analysis and Machine Learning methods. In this study, data and learning analyses from the HerbalDB database were obtained which obtained 1377 herbal compounds as candidate compounds for herbal drugs and then pharmacophore mapping with structural and ligand methods, the results of which will be evaluated for their antiviral content by molecular modeling methods [10].

Then, the next research is on the design of the 2019-nCov drug Machine Intelligent with the generative network complex (GNC) method. This study was conducted to discover an effective drug for 2019-nCov and it was found that the identities of the 2019-nCov and SARS-Cov proteases were almost identical with the similarity of 96.1%. Based on these results, the entire anti-SRAS-Cov chemotherapy has the potential to become 2019-nCov drugs [11]. After that, the next research is to combine data mining and biomedical technology to identify new drugs. The result of this research was the use of unsupervised pattern discovery method to discover new drugs using a database of ancient herbal compounds. The data used were 150 recipes and 255 herbal compounds that formed 42 clusters [12]. The determination of Covid-19 drug candidates has also been carried out using a search technique based on keyword symptoms or the name of the disease which is optimized with the Particle Swarm Optimization (PSO) algorithm as an Islamic medical engine framework design [13]. This research, however, still does not have a recommended value for the intensity of the composition of use from the results of the names of supplement ingredients in the form of herbal names based on the Qur'an and Hadith.

In determining the drug design of the Covid-19 and its new variants, this study uses an extreme genetic algorithm (eXGA), which is a combination of the Extreme Learning Machine (ELM) and Genetic Algorithm (GA), to optimize the design of the Covid-19

drug candidate according to the accurate composition value using historical Covid-19 data based on old and new variants. Such computation requires adequate servers for the preparation of software on the system.

2 Method

2.1 Determination of Drug Design for Covid-19 and Its New Variants

Coronavirus disease 2019 (Covid-19) and its several new variants such as Delta, Omicron and others are the names given by the World Health Organization (WHO) which were identified as originating from the corona virus which was first discovered in Wuhan, China at the end of 2019 [1]. Drug design is the process of finding new drug candidates based on the knowledge of biological targets. In its most basic sense, drug design involves the design of complementary molecules in the form and charge of target molecules that interact and bind to each other. Drug design can be determined by computer modeling techniques and bioinformatics approaches. Apart from small molecules and biopharmaceuticals, therapeutic antibodies are an increasingly important class of drugs and computational methods for increasing the affinity, selectivity and stability of these protein-based therapies which have also made great progress [14]. With computational modeling, it is expected that suitable AntiCovid-19 drug candidates can be discovered. The structure, signs of symptoms, and form of prevention of Covid-19 are shown as in Fig. 1.

Covid-19 has symptoms similar to other diseases such as flu, pneumonia, and allergies. Common symptoms of Covid-19 are fever, cough, sore throat, easy fatigue, shortness of breath, joint pain, headache, runny nose, stuffy nose, watery eyes, and diarrhea [2]. The structure of corona virus is shaped like a spike protein cube (S) as the main viral protein that connects the entry of the virus to host cells (receptors in host cells) [21]. In its development, Covid-19 mutated into new variants named Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.517.2), and Omicron (B.1.1.529) [20]. The emergence of new variants of COVID-19 makes the disease difficult to control because of differences in characters that make it spread more quickly and give rise to new symptoms that did not exist in the previous variants. Currently, the detection of the corona virus can only be identified by PCR test and antigen test. The types of covid-19 vaccines used in Indonesia include Moderna, Pzifer, AstraZeneca, Sinovac, and Sinopharm vaccines [21]. The new variants of COVID-19 lead to a decrease in the effectiveness of the vaccine

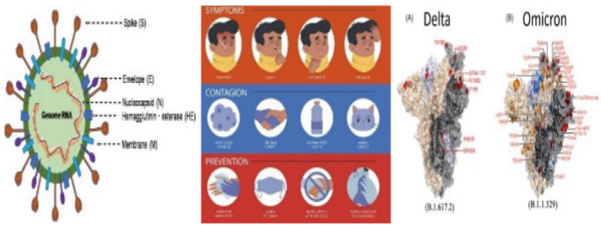


Fig. 1. Structure, signs and symptoms, and forms of prevention of Covid-19 and its new variants [15–20].

that has been inserted into the body. To date, there is no effective vaccine or drug for COVID-19 to prevent, eliminate, and treat this virus.

Other unique research related to prevention by vaccination and treatment of Covid-19 has been widely carried out. One of them is in the results of research conducted by Dr. Apt Valentina Yurina and several of her students from Pharmacy, Faculty of Medicine, Universitas Brawijaya (UB) regarding the development of a vaccine formulation that changes from injection to the arm muscle (intramuscular injection) to injection from the nose. Consequently, the user is more comfortable, has minimal risk of infection, and can do it independently. The intranasal vaccine uses Lactococcus lactis bacteria with the insertion of spike protein from the Corona virus, along with a mixed formulation of other ingredients, all of which are to stimulate immunity [22]. However, if the vaccine is not able to increase the immune system, then the way to cure the next patient is by administering modern drugs the design of which can be assisted by an intelligent computer system.

2.2 Meta-Deep AI Medicine Engine by Extreme Genetic Algorithm (ExGA)

Extreme Genetic Algorithm (eXGA) is a combination of ELM algorithm and Genetic Algorithm. Extreme Machine Learning Algorithm is a feedforward artificial neural network method that has a good learning speed. The learning process using the ELM method is divided into a training process and a testing process [23, 24]. Extreme Genetic Algorithm (eXGA) was built as a proposal and contribution to this research using a combination of technology to extract for reading the data, then performing the computation process, and then proceeding with the transfer of results. Systems built using this method can be run through Web and Mobile applications [24, 25].

In Fig. 2–3, the model algorithm, i.e., the Extreme Learning Machine (ELM), is utilized for fast predictive computing and the Genetic Algorithm (GA) for the problem-solving process with optimization. The modeling and optimization of covid-19 drug design are carried out by identifying Covid-19 variants. Then, the next step is performing feature extraction and learning by taking from the database of herbal and non-herbal medicines using the ELM method. Next, the step continues by optimizing the compound and the right dose by hybrid Islamic and evolutionary medicine for the Covid-19 and it is new variants drug candidate using a Genetic Algorithm with Geometric Time Variants as shown in Eq. 1 [25, 26], which is used to make adaptive values of Cr and Mr in each iteration with the limiting values of $c_{1\mathrm{i}} = 2.5$, $c_{1f} = 0.5$, $c_{2i} = 0.5$, and $c_{2f} = 2.5$ to balance the exploitation process and exploration in accelerating the discovery of optimal solutions.

$$Cr = c_2 = c_{2i}\left[\left(\frac{c_{2f}}{c_{2i}}\right)^{\frac{1}{t_{max}-1}}\right]^{t-1} \tag{1}$$

$$Mr = c_1 = c_{1i}\left[\left(\frac{c_{1f}}{c_{1l}}\right)^{\frac{1}{t_{max}-1}}\right]^{t-1} \tag{2}$$

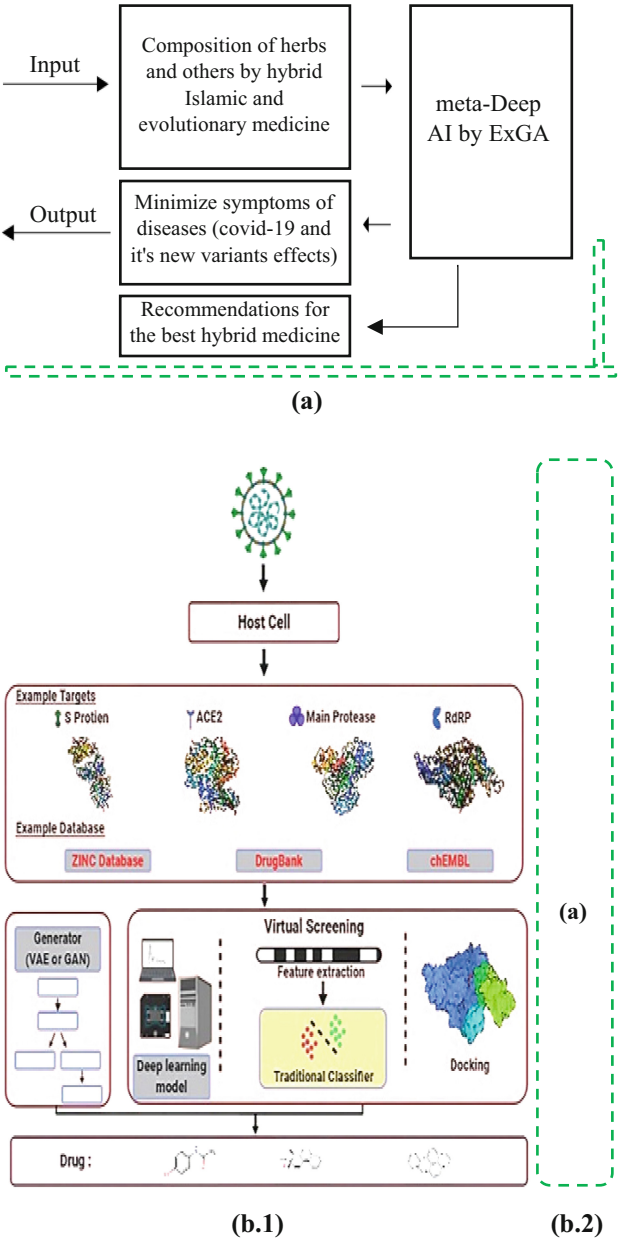


Fig. 2. (a) Diagram of meta-Deep AI Medicine Engine, (b.1) Illustration of Covid-19 [27] and (b.2) its new variants drug design based on the intensity of herbs and other on the patient's condition using ExGA (our contribution of this research)

ELM training process with bias:

1. Build W_{jk} as input weight and bias value b if any. The size of matrix b is [1 x j].
2. Calculate the output matrix of hidden layer $H = 1/(1+exp(-(X.W^T + ones(Ntrain,1)*b)))$. *Ntrain* is the number of training data.
3. Calculate output weight $\hat{\beta} = {}^{+}.Y$ where $H^{+} = (H^T.H)^{-1}.H^T$
4. Calculate $\hat{} = H.\hat{\beta}$

ELM testing process with bias:

1. Load W_{jk}, bias b value if any, and $\hat{\beta}$
2. Calculate $H = 1/(1+exp(-(Xtest.W^T + ones(Ntest,1)*b)))$
3. Calculate $\hat{} = H.\hat{\beta}$
4. Calculate the evaluation value, with MAPE, or others.

GTVGA process:

1. begin
2. $t = 0$
3. initialization $P(t)$
4. while (not terminated condition) do
5. reproduction $C(t)$ from $P(t)$ based GTV
6. evaluation $P(t)$ and $C(t)$ using Eq. 3
7. selection $P(t+1)$ from $P(t)$ and $C(t)$
8. $t = t + 1$
9. end while
10. end

ExGA algorithm process:

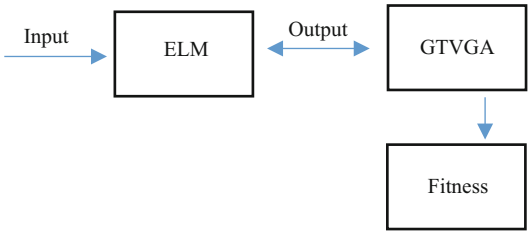
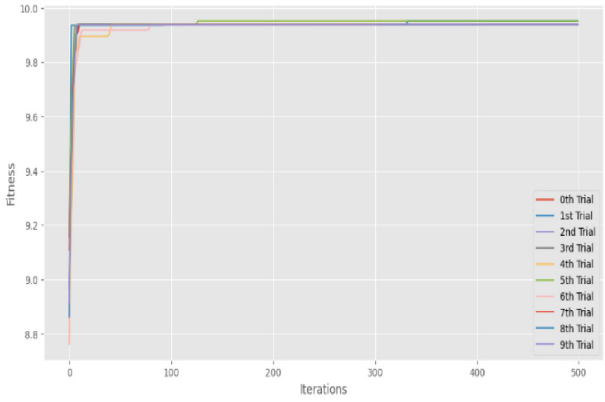
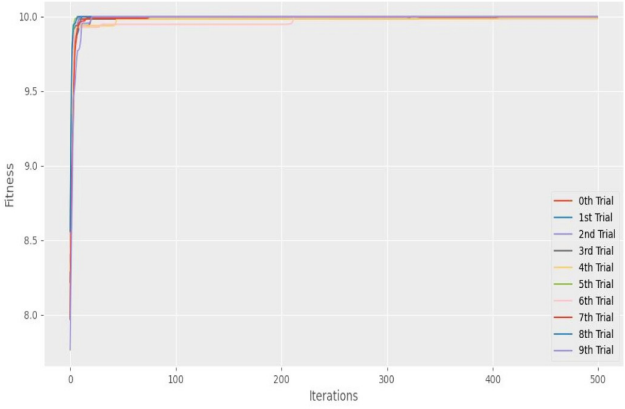


Fig. 3. Flow of ExGA Algorithm Framework (Integrated ELM with Geometric Time Variants Genetic Algorithm) [13, 23]



(a)



(b)

Fig. 4. Results of the system convergence graph Using (a) Arithmatic Time Variant (ATV), (b) Geometric Time Variants (GTV) GA & ELM

3 Result and Discussion

The dataset used in this study is 16 features of composition intensity from Herbs, Vitamins and Minerals, and 10 features of target symptoms for Covid-19 patients. The data consists of 34 data lines, with 2 types of groups, i.e., Treatment ($T1$ identifies the ones that have not been vaccinated which are 7 data; $T2$ represents the ones that have been vaccinated which are 28 data). The feature extraction learning process is carried out using the ELM method. The results of the learning are feature extraction or compound content and then the distance between the intensity values of the composition of the material as the percentage dose value will be generated randomly in

the optimization process using the Geometric Time Variants Genetic Algorithm, which has been implemented on https://github.com/imamcs19/Optimization-Drug-Design-by-Hybrid-Islamic-n-Evolution-Medicine-for-Covid-19-n-New-Var-with-GTVeXGA as a reference for the proof of testing results.

$$Fitness = \sum_{i=1}^{nTarget} \frac{1}{Val.\ of\ Targe\ t_i\ to\ Minimize} \tag{3}$$

Based on the results of the evaluation of the ExGA method using the fitness formula based on Eq. 3, very significant results were obtained. This can be analyzed from Fig. 4 which shows the results of the convergence of evaluation values from several trials of drug candidate models that have been discovered, where GTV is better than ATV.

4 Conclusion

The results of the tests carried out several times showed convergence results. The more iterations used, the better the results with smaller error values generated. These results show that the Extreme Genetic Algorithm (eXGA) provides optimal results in determining the dosage of compounds from drug candidates for many diseases, especially in this study which focuses on COVID-19. To test the effectiveness of the results of this modeling, trial tests on animals can be carried out before being given to humans. In this study, it is limited to the manufacture of drug designs. With the eXGA method, drug design modeling using metaheuristic techniques makes complex computations easier in this case.

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