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Steroids and Triterpenes: Potential drug candidates for COVID-19

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ABSTRACT: ***World Health Organisation declared the Novel Corona Virus as a pandemic disease on 11th March 2020. Corona Virus or Severe Acute Respiratory Disorder Corona Virus 2 (SARS CoV2) caused a situation of panic all around the globe as well as a huge economic disturbance faced by all the nations. Currently there is no medicine approved for this disease that can overcome the human suffering. Although, drugs like hydroxychloroquine have been used to treat the patients but they are nor so effective and beside they causes several severe side effects. This lack of treatment increases the urgency of efficient and safe treatment. Traditionally, natural products have been used to cure various viral diseases like HIV, MERS-CoV, and influenza. Medicines made from purified natural products can help to prevent as well to treat the patients that are suffering from the corona virus. Therefore, current review discusses the potential of triterpenes and sterols found in the natural products that have been well established against various viral diseases. Interestingly, it has been found out that some plants products have the potential and they can be used as the potent drug candidates for the development of the anti-viral against the Corona Virus.***

Keywords: Antiviral, Corona Virus, Natural Product, Steroids, Triterpenes, Pandemic.

INTRODUCTION

Steroids and triterpenes are known to be common groups that are present in numerous natural marine and terrestrial origins (e.g., plants, animals, and microorganisms). In addition, with tremendous chemical diversity, they contain several sub-classes. Since the invention of digoxin in 1785, such as cortisol, fusidic acid, carbenoxolone, and β-Aescin, these two groups of compounds have been supplied with several effective drugs for various ailments [1]. These substances have a range of biological functions, including digoxin used as topical antibiotics in the treatment of heart problems and atrial fibrillation and fusidic acid. Carbenoxolone improves the susceptibility of peripheral insulin and therapies for gastric ulcer and β-Aescin used in the management of SMMC-7721 cells of human hepatocellular carcinoma. Steroids and triterpenes have different possible antiviral effects, like the activity of the anti-Herpes simplex virus, the activity of anti-hepatitis B, anti-HIV1 and 2, Helps, and the activity of the hepatitis C virus. The class of steroids comprises of 25 chemical subcategories, with around 11,825 earlier described compounds. Although the compound class of triterpenoids comprises of 47 chemical subcategories with around 18,864 chemical compounds already isolated from various biological compounds [1].

For a broad spectrum of pharmacological activity, several members from both groups were identified. Current review provides an opportunity to reflect on the antiviral ability of these significant secondary metabolites groups. The study also examined the possibility of these tested triterpenes and sterols to provide promising candidates for the production of successful therapies for the emerging SARS-CoV-2 pandemic against the currently available protein targets.

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DISCUSSION

Anti-HIV Candidates

Sterol and triterpenes have been published extensively in the literature as anti-HIV agents, demonstrating several modes of action as antiviral drugs. Reverse transcriptase is a crucial enzyme that is deemed essential for viral replication in retroviruses such as HIV, and is thus extensively tested for the implementation of antiHIV therapeutics. During the last 20 years, numerous sterols and triterpenes have been identified as effective HIV reverse transcriptase inhibitors. Table 1 is representing the potent HIV agents that can be further studied.

Table 1. Anti-HIV candidates for the development of drugs against Corona Virus

Anti-HIV candidate	Origin	IC50
Stigmastanol	Rice Bran	3.9 Mm
Clathsterol	Clathria Species	10µm
A, B- Amyrenone	Burseraceae Family Species	3.3 µm
Bryonolic Acid	Family Cucurbitaceae	5.3 µm
Isotirucallol	Camellia. Sasanqua	3.5 µm
Butyrospermol	Camellia Japonica	3.1 µm
Calenduladiol	Calendula Officinalis	5.4 µm
Erythrodiol	Olea Europaea	5 µm
1β-Hydroxyaleuritolic Acid 3-P-Hydroxybenzoate	Maprounnea Africana	3.7 µm
Lupeol	Edible Vegetables And Fruits	3.8 µm
Salaspermic Acid	Triterygium Wilfordii.	10 µm
Uvaol	Callicarpa Bodinieri	9.5 µm

Protease Inhibitor

Specific viral hydrolytic enzymes are proteases. Typically, they are included in viral entry and activation of the mechanism of viral replication. In addition, the majority of infectious viruses in their host receptor binding and entrance use other human-based proteases. Pan-protease inhibitors have therefore demonstrated wide ranging antiviral activity, including that of the recent SARS-CoV-2 outbreak.

Ganoderma species have demonstrated in vitro inhibitory activity towards HIV-1 protease with certain lanostane-type triterpenes obtained from medicinal mushrooms. For instance, 3β-5 alpha-dihydroxy-6β-methoxyergosta-7,22-diene was obtained and identified as an effective non-competitive HIV-1 protease inhibitor (IC50 = 7.8 µM) from an edible mushroom species called *G. lucidum*. In fact, 3 triterpenes of the *G. colosum*-derived lanostane type, named

colossolactones E, G, and V, showed anti-HIV-1 protease with IC50 values ranging from 4.5 to 8.5 μM, respectively. Also uvaol also found to inhibit the HIV-1 protease [2].

DNA Polymerase Inhibitors

The Maprounnea africana-derived pentacyclic triterpene,1β-hydroxyaleuritolic acid 3-p-hydroxybenzoate has been also reported effective inhibition action against DNA polymerase with IC50 equal to 7.5 μM in relation to its anti-HIV-1 reverse transcriptase activity. Table 2 is representing a list of replication inhibitors which can be further studied for the development of drugs to target the corona virus.

Table 2. Replication inhibitors which have potential for anti Corona Virus drugs

Replication Inhibitors	Origin	Activity
β-Aescin	Aesculus hippocastranum	Inhibits NF- Ƙb Activation And Cytokines Production
Asiatic acid	Actinida argute , Centella Asiatica , Combretum laxum	Influences Many Enzymes, Receptors, Growth, And Transcription Factors
lactone lancilactones C	Kadsura lancilimba (Schizandraceae),	Inhibited HIV Replication
Oleanolic acid (OA)	In more than 1600 different plant species	Inhibit HIV-1 Replication In Acutely Infected H9 Lymphocyte Cells
Platanic acid	Syzigium claviflorum (Myrtaceae)	Inhibition Of Uninfected H9 Cell Growth
Salaspermic acid	Triterygium wilfordii	Anti-HIV Replication In H9 Lymphocyte Cells
suberosol	Polyalthia suberosa (Annonaceae)	HIV Replication In H9 Lymphocyte Cells

Other Compounds with Antiviral Activity

Several other compounds have been identified that represents the antiviral potential and can further be used to treat the SARS CoV2. Table 3 is representing a list of compounds that represents potential [3].

Table 3. Compounds that represents the antiviral properties

Compound	Class	Origin
Halistanol sulfate F and halistanol sulfate G	Steroid sulfate oxoanions	Psedaxinissa digitate
orthoesterol A, B and C disulfate	Sterol disulfate orthoester	Petrosia weinbergi
Alphitolic acid	Ursan-type pentacyclic triterpene	Rosa woodsii

Betulinic acid (BetA)	Pentacyclic lupine type triterpene	Sizigium claviflorum
Dammaradienol	Seco-dammarane type triterpenes	Balanocarpus heimii (Dipterocarpaceae) and Dipterocarpus alatus resin
Dammarenolic acid	Seco-dammarane type triterpenes	Balanocarpus heimii (Dipterocarpaceae) and Dipterocarpus alatus resin
Hydroxydammarenone I	Seco-dammarane type triterpenes	Balanocarpus heimii (Dipterocarpaceae) and Dipterocarpus alatus resin
Hydroxyhopanone	Seco-dammarane type triterpenes	Balanocarpus heimii (Dipterocarpaceae) and Dipterocarpus alatus resin
Glycyrrhizin	Triterpenoid saponin glycoside	Glycyrrhiza glabra
Pomolic acid	Pentacyclic ursane-type triterpenoid	Rosa woodsia
Pristimererin,	Quinone-methide	Triterygium regelii
Tingenone	Quinone-methide	Triterygium regelii
Iguesterin	Quinone-methide triterpenes	Triterygium regelii
Saikosaponins	Glucosides	Bupleurum spp., Heteromorpha spp., and Scrophularia scorodonia. Saikosaponins (A, B_2, C, and D)

CONCLUSION

Sterols and triterpenes are an enormous class of compounds with numerous pharmacological processes, primarily anti-cancer, anti-inflammatory, immunomodulatory and anti-viral compounds. In this study, we concentrated on the natural or derivatized antiviral targets that demonstrated powerful actions as anti-HIV and demonstrated their processes of actions that can connect these compounds to be a powerful hit for the management of COVID-19. It can be inferred that certain compounds, such as 1β-Hydroxyaleuritolic acid 3-p-hydroxybenzoate, which serve as reverse transcriptase inhibitors, may be a strong match for SARS-2, while at the same moment have also shown a protease inhibitor. Lupeol and Uvaol demonstrated effective reverse transcriptase inhibitors in the same way. Salaspermic acid has shown reverse transcriptase inhibition effect towards HIV and has replication inhibitory effect. n the other hand, referring to replication inhibitors, β-Aescin is claimed to be the one of choice, as it has been stated to suppress NF-ƙB stimulation and development of cytokines.

A few of the sulfated sterols, such as halistanol sulphate F and halistanol sulphate G, demonstrated anti-HIV-1 antiviral properties, that might indicate the sulphate group's significance in virus suppression. Alphitolic acid has been shown to have an action somewhat close to that of dexamethasone in inhibiting nuclear factor kappa-B (NF-1B) or in blocking the

production of pro-inflammatory cytokines like cytokines. The alphitolic acid suppressor activity can serve to minimise the severity of COVID-19-associated inflammatory syndrome. The preceding section indicated that not only triterpenes are involved, but also their semi-synthetic derivative, such as betulinic acid, have been tested towards influenza A, herpes simplex type 1 (HSV-1) and ECHO-6 enterovirus as the antiviral of betulinic acid and its derivatives. Glycyrrhizin is among the most prevalent triterpenes and its metabolites, like glycyrrhetic acid (GA), have been documented to be capable of inhibiting the cytopathic effect of various DNA and RNA viruses, like vaccinia, HSV-1, Newcastle disease, and also in vitro vesicular stomatitis (VSV). It has been found by many researchers that M^{Pro} is the perfect target to develop drug, it was reported that pristimererin, tingenone, and iguesterin have the potential and then might show the anti Corona Virus properties.

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