**Supplementary Tables**

**Supplementary Table 1. Nucleoside analogues from marine sponge as a lead for the development of antiviral drugs.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Nucleotides analogues** | **Marine sponge** | **Structural modification** | **Antiviral activity** | **Lead antiviral drug** |
| **Spongouridine and spongothymidine**  | *Cryptotethya sp*  | * Sugar part
* Arabinose with inverted OH
 | Antiviral activity [1]. | * Cytarabine Ara-C (spongocytidine)
* Vidarabine Ara-A

(sphongoadenosine)* Inspired acyclic analogues in the development of (azidothymidine AZT) drug [2].
 |
| **1-Methylisoguanosine** | *Tedania digitata* [3] | Methylated nucleobase  | Antiviral agent [4]. | Acyclovir (N-alkylated) acyclic guanosine [5]. |
| **Kumusine**  | *Theonella cupola* [6]. | Chloro-adenosine analogues | It showed moderate immunosuppressive activity (1). | Halogenated nucleosides are common synthetic analogues [7]. |
| **Trachycladine A, B** | *Trachycladus laevispirulifer* [8]. | * Deoxynucleoside and methylated nucleoside
* Trachycladine B halogenated derivatives.
 | No reported antiviral activity | NA |
| **Aplysidine**  | *Aplysina sp* [9] | Theophylline (1,3-dimethyl-xanthine) analogue  | No reported biological activity  | Inspired the synthesis of theophylline antiviral agents [10; 11]. |
| **Doridosine**  | * *Tedania digitata*
* *Anisodoris nobilis*
 | Methylated isoguanine  | Anti-inflammatory activity | Synthetic alkylated isoguanine derivatives [12]. |
| **P10 [13]**  | *Theonella swinhoei* [14] | * Peptidyl nucleosides analogues
* Amide analogues of blasticidin S
 | * Antiviral activity [15].
 | Conjugated structures  |
| **3-Methyl-2'-deoxycytidine, and 3-Methyl-2'-deoxyuridine**  | *Geodia baretti* [16] | * Methylated nucleobase
* Deoxy sugar
 | * Antiviral activity [17]
* No detailed report on its biological activity.
 | * Inspired methylated sugar with antiviral activity.
* 2`-c-methyl cytidine with antiviral activity against COVID-19 [18].
 |
| **Tubercidin** | *Caulospongia biflabellata*[19; 20] | * 7-Deaza-adenosine
* C-5 substituted tubercidin analogues showed significant reduced toxicity [21].
 | * Broad spectra antiviral activity against RNA virus
 | * MK-608 antiviral drug [22]
* Deaza-adenosine analogues and methylated sugar.
 |
| **(5-Iodo-5'-deoxytubercidin) and 4-amino-5-bromopyrrolo[2,3-d]pyrimidine**  | *Hypnea valendiae* [7] | Halogenated tubercidin derivatives  | Antiviral activity [23]. | Privileged scaffold in the design of antiviral nucleosides [23; 24]. |
| **2′,3′-Didehydro-2′,3′dideoxyuridine** | *Aplysina sp.* | Unsaturated deoxy sugar part  | Antiviral activity [25]. | Unsaturated antiviral drugs stavudine, elvucitabine and abacavir [26]. |
| **8-Oxoisoguanine-nucleotides** | *Clathria strepsitoxa* [27] | * Modified base with 8-oxa and 1-methyl [28].
* Acetylated sugar
 | Not screened for its antiviral activity. | NA |
| **Mycalisines A and B** | *Mycale sp.* [29] | * Modified adenine and guanine base with cyano-moiety
* Modified sugar with exocyclic double bond [28].
 | Scaffold for the design of antiviral drugs.  | Remedisivir  |
| **N3,5-Cycloxanthosine** | *Eryus sp* | First natural occurrence cyclo-nucleoside [30]. | Reported antiviral properties against different human viruses [30]. | Cyclonucleosides (2,5¢-*O*-cyclocytidine) patented antiviral agent [31]. |
| **Avinosol** | *Dysidea sp* | A meroterpenoid-nucleoside conjugate | Anti-invasion activity [32] | Inspired betulinic acid nucleoside conjugate with potent antiviral activity [33] |
| **Pyridine α-riboside and α-nicotinamide riboside (Neopetrosides A, B) [34]** | * *Neopetrosia sp* [34]
* *Protophlitaspongia aga*
 | Modified pyridine nucleosides are naturally rare. | * Lead for antiviral drug design [35]
* Nicotinamide scaffold with reported antiviral [36].
 | Inspired pyrimidine derivatives as:* Favipiravit (T-705)
* Sofosbuvir [37]
 |
| **Ilimaquinone and Asmarine B** | * *Smenospongia sp* [38]
* *Raspailia sp* [39]
 | Asmarine B [38] has adenosine that replaces the quinone moiety in ilmaquinone. | * Reported antiviral [39]
* Computational modeling showed that Ilimaquinone as a promising inhibitor for SARS-CoV-2 [40].
 | Ilimaquinone derivatives as antiviral agent [41]. |
| * **2-Deoxyuridine, 2-deoxyinosine, and 2-Deoxyadenosine**
* **2′-Deoxy-guanosine**
* **Deoxycytidine**
* **Methyl-2'-deoxyuridine**
 | * *Callyspongia sp [42]*
* *Haliclona sp* [43]
* *Geodia baretti* [16]

Dragmacidon coccinea [44] | Deoxy sugar nucleosides. | Deoxy nucleoside with antiviral activity.[45] | * Remedisivir with cyano deoxy sugar
* Gemecitabine deoxy fluoro sugar
* Sofosbuvir with deoxy sugar
 |

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