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Research Article

Design, Synthesis, and Biological Activity Evaluation of Novel AZT and Adenosine-Derived 1,2,3-Triazoles

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$CuSO_4$/hydrazine hydrate was used as a catalyst system for copper(I)-catalyzed alkyne-azide cycloaddition (CuAAC) of AZT and 5′-azido adenosine with terminal alkynes to give 30 novel 1,2,3-triazole derivatives. Screening for their anticancer, anti-inflammatory, angiotensin-converting enzyme 2 (ACE2), and 3C-like protease ($3CL^{pro}$) inhibitory activities showed that several triazoles of AZT containing murayafoline A and indirubin-3′-oxime inhibited the growth of HepG2 and LU-1 with the IC_{50} values ranging from 11.01 to 19.87 μg/mL. Besides that, some triazole derivatives of adenosine exhibited anti-inflammatory activity against RAW264.7 cells with the IC_{50} values within an interval of 12.00–59.48.00 μg/mL. Especially, two triazoles of adenosine with indirubin-3′-oxime at *O*- and *N1* positions expressed the ACE2 and $3CL^{pro}$ inhibitory activities in which the triazole of adenosine with indirubin-3′-oxime at *N1* inhibited both ACE2 and $3CL^{pro}$ inhibitory activities with IC_{50} values of 135.62 and 142.95 μg/mL, respectively.

1. Introduction

Nowadays, linking two biologically active moieties together is one of the fields that are receiving much interest in pharmaceutical chemistry [1]. Some of the reactions commonly used effectively for this purpose include the Suzuki, Heck reactions [2–5], alkylation [6, 7], esterification [8, 9], and copper(I)-catalyzed alkyne-azide cycloaddition (CuAAC) [10–14]. Among the reactions mentioned, the CuAAC reaction is one of the most powerful methods for generating new conjugates through 1,2,3-triazole linkage [15]. Up to now, this reaction is within the concept of click chemistry and is evaluated as the simplest and the most effective method [16, 17]. It has a wide scope of applications [18], even in living organisms without requiring harsh conditions. For this reason, click chemistry along with bioorthogonal chemistry won the Nobel Prize in Chemistry in 2022 [19]. According to studies, 1,2,3-triazoles not only act as a linker or bioisostere but also themselves are a pharmacophore of various biological activities such as cytotoxic [20, 21], antimicrobial [22], anti-inflammatory [23], antianesthtic and antioxidant [24], and antiviral [25, 26] activities. More recently, several 1,2,3-triazole derivatives were also reported as potential for anti-SARS-CoV-2 activity [27–29]. Chemically, the 1,2,3-triazole ring also possesses many interesting features, such as high stability in both acidic and basic media, high dipole moment, capacities of forming hydrogen bonds with hydrogen donors, π-π

interactions with aromatic rings, or coordination bonds with metal ions [30, 31]. These properties are useful for molecular docking to predict the mechanism of action to target protein and interpret the structure-activity relationship [32].

Nucleosides play an important role in building the structural block of RNA and DNA and are responsible for energy transmission, preservation, and transmission of the genetic information of all living creatures [33, 34]. In addition, they are also responsible for biological energy storage and transmission, signaling, and regulation of various aspects of metabolism and even play an important role in an antioxidant [35, 36].

In pharmacology, nucleosides are also used as templates to design compounds for medicinal purposes. A large number of compounds containing nucleosides are approved to be drugs for the treatment of various diseases; among nucleoside drugs, half of them are antiviral and a quarter are anticancer [37]. In these cases, nucleoside scaffolds are required to exhibit biological activities as expected; for example, zidovudine moiety (**1**) is necessary to design its derivatives for anti-HIV activity [38], adenosine (**2**) is an important structural part of ATP (**3**), and it is also a required structure in 5′-(*α*,*β*-methylene)diphosphonate adenosine (APCP) (**4**) to exhibit anticancer activity due to the inhibition of CD73 enzyme overexpression [39]. The structures of compounds (**1**), (**2**), (**3**), and (**4**) are shown in Figure 1. Moreover, adenosine acts as an antagonist, responsible for protecting cells from stress-induced factors by interacting with its receptor (AR), and adenosine receptors are distributed throughout the body and are implicated in several diseases such as CNR disorders, cancer, heart disease, inflammation, and lung disease; therefore, ARs are always an attractive therapeutic target for scientists [40]. Because of such important roles, adenosine is an interesting nucleoside that can be used to design its 1,2,3-triazole derivatives for various biological activities; for example, several adenosine 1,2,3-triazole derivatives with biotin have been synthesized and tested for inhibitory activity against *S. aureus* and biotin protein ligase [41], and others have displayed as A_3AR agonists with high affinity and selectivity to the A_3 adenosine receptor [42, 43]. The receivable diversity in structure and biological activities of triazole compounds prompts us to continue studies in this area. Therefore, in the present work, we introduce the design and synthesis of novel AZT and adenosine 1,2,3-triazole derivatives and their anti-inflammatory, cytotoxic, ACE2, and SARS-CoV-2 inhibitory activities.

2. Results and Discussion

2.1. Chemistry. The 1,2,3-triazoles of AZT and adenosine are formed by the CuAAC reaction of their azides with terminal alkynes (Schemes 1 and 2). While 3′-azidothymidine **1** (AZT) is commercially available, 5′-azido adenosine **6** is prepared from 5′-tosyl adenosine **5** by a nucleophilic substitution reaction with NaN_3 in DMF at 50°C for 24 h (Scheme 2).

Terminal alkynes **9a**–**q** were prepared by the reactions of alkylation and amidation of starting compound including 6-hydroxy-2-methylquinazolinones **8a**–**g**, 1-hydroxy-3-methy lcarbazole **8h**, indirubin-3′-oxime **8i**, 4-hydroxyphen ylacetamide **8j,** acridone **8k**, murrayafoline A **8l**, indirubin **8m**, acridone acetic acid **8n**, 3,4,5-trimethoxybenzoic acid **8o**, 4-methoxyphenylacetic acid **8p**, and ketoprofen **8q**. First, 6-propargyloxy-2-methylquinazolinones **9a**–**g** were prepared from 6-hydroxy-2-methylquinazolinones which were synthesized from 5-hydroxyanthranilic acid according to a published procedure by Vu et al. (Scheme 1) [44].

The hydroxy group of 6-hydroxy-2-methylquina zolinones was then alkylated with propargyl bromide in DMF in the presence of weak base K_2CO_3 to give 6-propargyloxy-2-methylquinazolinones **9a**–**g** in 72–76% yields (Scheme 3). Next, the synthesis of terminal alkynes **9h**–**i** was documented in our previous studies [45, 46]. This procedure was also used for the *O*-alkylation of 4-hydroxyphenyl acetamide **8j** with propargyl bromide to obtain new 4-propargyloxyphenylacetamide **9j** in 90% yield (Scheme 2).

For *N*-propargyl compounds, the amine groups of acridone **8k**, murrayafoline A **8l**, and indirubin-3′-oxime **8m** were also converted into the corresponding *N*-propargyl groups by propargylation reactions as described by Tai [45] and Dan [46]. Last but not least, amides **9n**–**q** containing *N*-propargyl groups were prepared from corresponding acids **8n**–**q** using a known protocol of Tai et al. [45].

The structures of new terminal alkynes were determined by ^{1}H-, ^{13}C-NMR, and HRMS spectra. Their ^{1}H-NMR spectra indicated the presence of a propargyl group by the signal of two protons in -CH_2- in the region of 3.84–4.95 ppm (d, $J = 2.4$ Hz), and an alkyne proton caused a triplet to rise from 3.07 to 3.61 ppm (t, $J = 2.4$ Hz). The signals of carbons in this group were also found and assigned. Particularly, the signals of methylene carbon (-CH_2-) had chemical shifts within the regions of 55.3–60.1 ppm (-CH_2-) for *O*-propargyl compounds and 27.9–28.1 ppm for *N*-propargyl compounds, The signals of quaternary carbon (-C≡) and methine carbon (≡CH) resonated within the regions of 78.7–80.1 ppm and 78.0–78.8 ppm, respectively. The NMR and HRMS data agreed well with their structures.

In the final step, terminal alkynes **9a**–**q** were cyclized with AZT **1** and 5′-azido adenosine **6** by a CuAAC reaction to produce target 1,2,3-triazole derivatives **10a**–**m** and **11a**–**q**. First, CuI was directly employed to catalyze for this reaction in DMSO, THF, and DMF in the presence or absence of diisopropylethylamine; however, TLC showed no product formation. Similar results were also observed with the catalysis of $CuSO_4$/sodium ascorbate in *n*-butanol or DMF. Finally, $CuSO_4$/hydrazine hydrate [47] was found to be the effective catalyst to couple terminal alkynes **9a**–**q** with both AZT **1** and 5′-azido adenosine **6** in CH_3CN: H_2O 1 : 1 v/v. Precipitates **10a**–**m** and **11a**–**q** were stirred in EDTA 1M solution overnight, then filtered on a Buchner funnel, and washed thoroughly with water to remove Cu (II) ions. Crude 1,2,3-triazole derivatives were purified by column

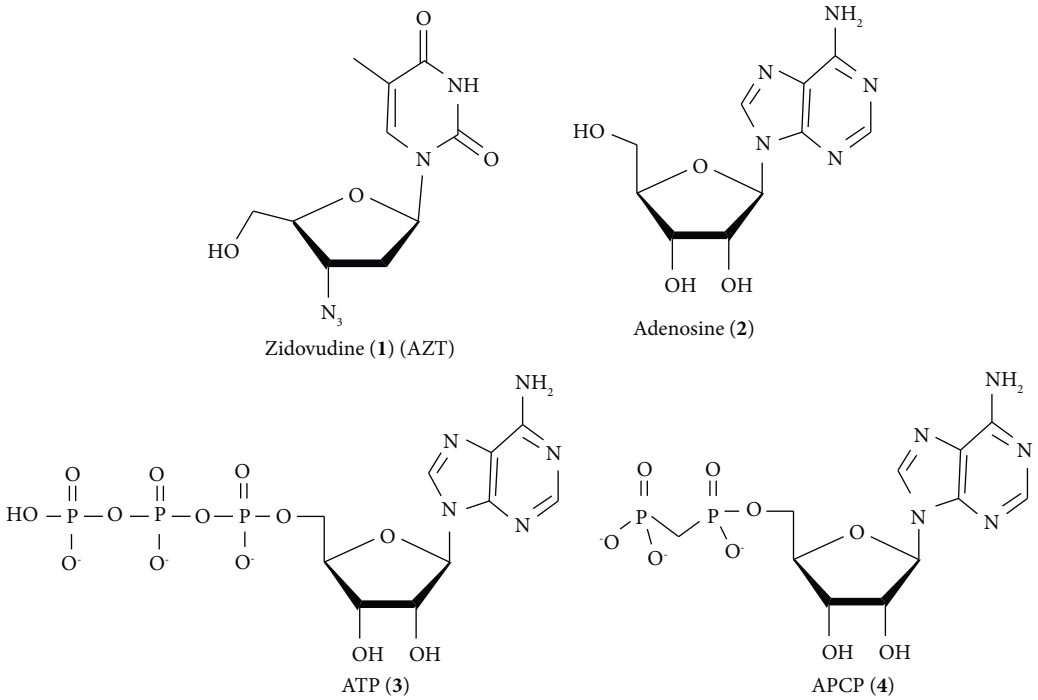
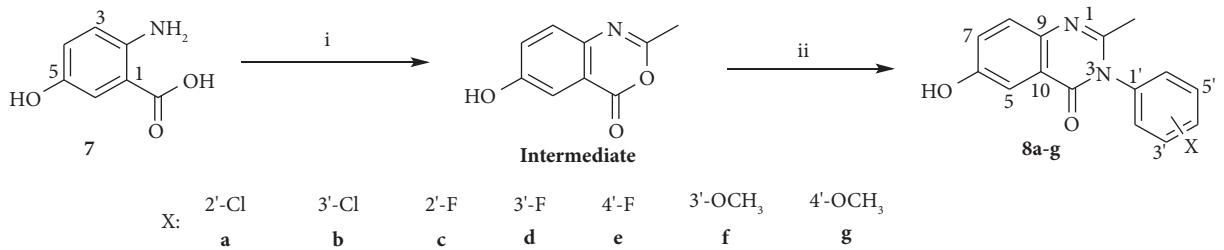


Figure 1: Structures of AZT (1), adenosine (2), ATP (3), and inhibitor of CD73 enzyme AOPCP (4).



Scheme 1: Synthesis of 6-hydroxy-2-methylquinazolinones **8a**–**g**. Reagents and conditions: (i) $(CH_3CO)_2O$, reflux 2 h; (ii) substituted arylamines, CH3COOH, 14 h.

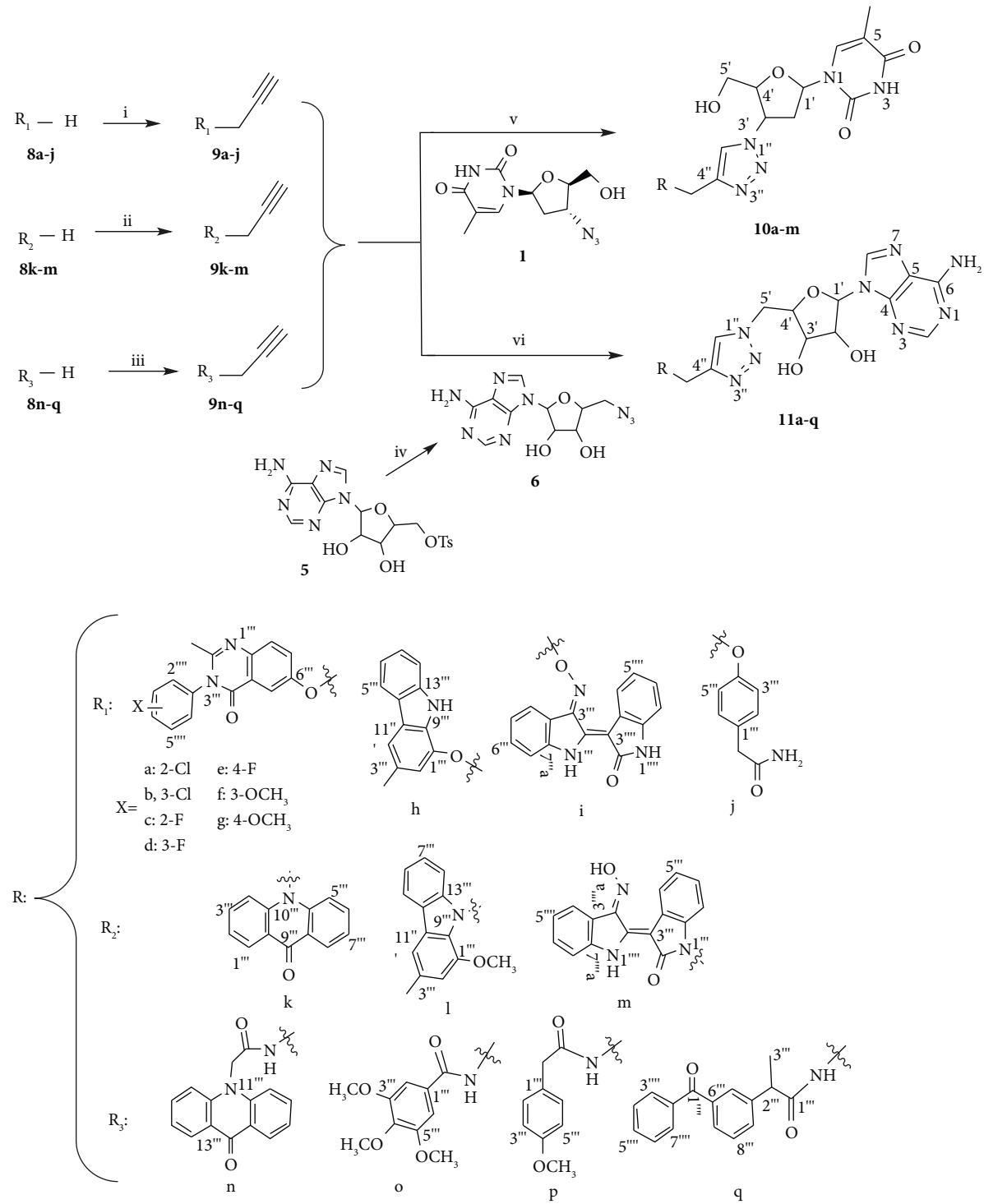
chromatography/silica gel eluted with CH_2Cl_2:MeOH to give designed products **10a**–**m** and **11a**–**q** in 35–55% yields (Scheme 2).

In the case of **10m**, the CuAAC reaction produced two isomers **10m1** and **10m2** (Figure 2) that were recognized by pairs of signals in its ^{1}H-and ^{13}C-NMR spectra; for example, a pair of signals H-1′ in pentose moieties (t, $J = 6.6$ Hz) in its ^{1}H-NMR was observed at 6.51 and 6.45 ppm, respectively. This could confirm the existence of two isomers **10m2** and **10m1** which had roughly 40% of **10m2**-isomer and 60% of **10m1**-isomer, corresponding to 0.67 for the **10m2**/**10m1** ratio based on its ^{1}H-NMR spectrum.

The structures of target products were elucidated by ^{1}H-, ^{13}C-NMR, and HRMS spectra. In their NMR, the signals of protons and carbons were similar to those in the NMR of **9a**–**q**, AZT, and adenosine; however, the signals of acetylene moieties in **9a**–**q** were replaced by those of protons and carbons in the 1,2,3-triazole ring. Especially, the signals of H-5″ in the triazole ring were observed by the singlet ranging from 7.20 to 7.30 ppm. The chemical shift of C-4″ and C-5″ was found in the regions of 141.9–144.8 ppm and 122.7–124.5 ppm for the 1,2,3-triazoles of AZT (**10a**–**m**) or 144.8–144.7 ppm and 123.4–128.8 ppm for the 1,2,3-triazoles of adenosine (**11a**–**q**). The NMR and HRMS data were in excellent agreement with their structures.

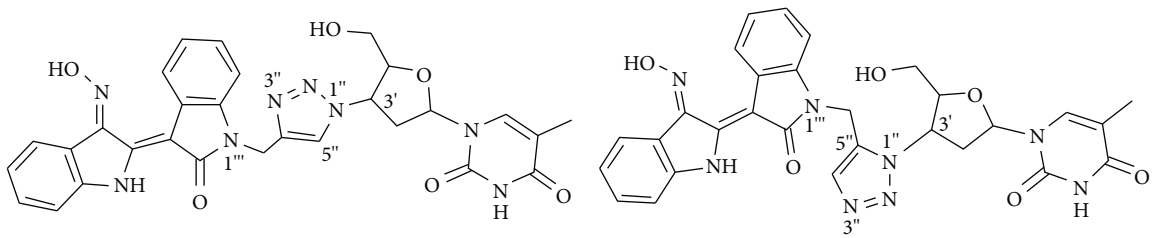
2.2. Biology

2.2.1. Anti-Inflammatory Activity. The *in vitro* anti-inflammatory activity of the prepared products was tested by measuring reduced NO production in LPS-stimulated RAW 264.7 cells. The result in Table 1 shows that seven compounds including **10g**, **11a**, **11j**, **11n**, **11o**, **11p**, and **11q** expressed NO production inhibition with the IC_{50} values ranging from 12.00 ± 0.01 to 67.67 ± 0.14%, while triazoles **10h**, **10j**, and **11d** were found to be toxic to RAW 264.7 cells. Notably, all four click products **11n**–**11q** derived from 3,4,5-trimethoxybenzoic acid, acridone acetic acid, 4-methoxyphenylacetic acid, and ketoprofen exhibited an anti-



Scheme 2: Synthesis of AZT and adenosine 1,2,3-triazole derivatives **10a–m, 11a–q**. Reagents and conditions: (i) propargyl bromide, K_2CO_3, DMF; (ii) propargyl bromide, NaH, DMF, 0°C-rt, then HO-NH_2.HCl, pyridine for **9m**; (iii) propargyl amine, DCC, TEA, DMAP, −20°C-rt; (iv) NaN_3, DMF, 50°C, 24 h; (v) AZT, $CuSO_4/N_2H_4.H_2O$, CH_3CN:H_2O 1 : 1 v/v, rt, 3h; (vi) 5′-azido adenosine, $CuSO_4/N_2H_4.H_2O$, CH_3CN:H_2O 1 : 1 v/v, rt, 3 h.

inflammatory effect on RAW 264.7 cells; among them, compound **11q** formed from the anti-inflammatory drug ketoprofen was the most potent with an IC_{50} value of 12.00 μg/mL. Presumably, the presence of an amide bond -CONH- seems to be beneficial for anti-inflammatory activity. Finally, the results in Table 1 also suggest that adenosine was not a substrate to design its derivatives for anti-inflammatory purpose.



10m1 **10m2**

Figure 2: The structures of two isomers **10m1** and **10m2.**

Table 1: Anti-inflammatory activity of the prepared products.

No	Compounds Positive control**	IC_{50} value* (μg/mL) 0.61 ± 0.02
1	10a	>100
2	10b	>100
3	10c	>100
4	10d	>100
5	10e	>100
6	10f	>100
7	**10g**	**43.48 ± 0.17**
8	10h	>100
9	10i	>100
10	10j	>100
11	10k	>100
12	10l	>100
13	10m	>100
14	**11a**	**23.69 ± 0.04**
15	11b	>100
16	11c	>100
17	11d	>100
18	11e	>100
19	11f	>100
20	11g	>100
21	11h	>100
22	11i	>100
23	**11j**	**59.20 ± 0.11**
24	11k	>100
25	11l	>100
26	11m	>100
27	**11n**	**59.48 ± 0.06**
28	**11o**	**51.84 ± 0.15**
29	**11p**	**67.67 ± 0.14**
30	**11q**	**12.00 ± 0.01**

*Data represent the mean ± standard deviation of three independent wells.
**Positive control: cardamonin (Merck, Germany).

Table 2: *In vitro* cytotoxic activity of the synthesized conjugates.

No	Comp.	IC_{50} value* (μg/mL)	
		HepG2	LU-1
	Positive control**	0.29 ± 0.01	0.32 ± 0.02
1	10a		
2	10b		
3	10c		
4	10d		
5	10e		
6	10f		
7	10g		
8	**10h**	**19.30 ± 0.60**	**11.01 ± 0.15**
9	**10i**	—	**12.74 ± 0.42**
10	10j	—	—
11	10k		
12	10l		
13	**10m**	**19.87 ± 0.25**	**11.07 ± 0.08**
14	11a	—	—
15	11b	—	—
16	11c	—	—
17	11d	—	—
18	11e	—	—
19	11f	—	—
20	11g	—	—
21	**11h**	**19.74 ± 0.37**	—
22	11i	—	—
23	11j	—	—
24	11k	—	—
25	11l	—	—
26	11m	—	—
27	11n	—	—
28	11o	—	—
29	11p	—	—
30	11q	—	—

*Data represent the mean ± standard deviation of three independent wells.
*Ellipticine (Merck, Germany) was employed as a positive control.

2.2.2. Cytotoxic Activity. All prepared products were also evaluated for cytotoxic activity against HepG2 and LU-1 cell lines. The obtained result in Table 2 reveals that only four triazole derivatives **10h**, **10i, 10l,** and **11h** exhibited moderate cytotoxic activity with the IC_{50} values ranging from 11.01 to 19.87 μg/mL. Among them, AZT triazoles **10h** and **10m** inhibited the growth of both tested cell lines HepG2 and LU-1 with the IC_{50} values of 19.30, 11.01 and 19.87, 11.07 μg/mL, respectively. Clearly, this result is reasonable since adenosine is a nucleoside with no cytotoxic activity.

2.2.3. ACE2 and 3CL^{pro} Inhibitory Activities. As far as we know, ACE2 is a potential binding site for the virus spike protein of SAR-CoV-2 and plays a vital role in the SAR-CoV-2 infection [48], while 3CL^{pro} is essential for SAR-CoV-2 replication but has not been present in host cells [49]. Thus, ACE2 and 3CL^{pro} have recently emerged as excellent targets for the design of anticoronaviral compounds [49, 50]. For screening of both ACE2 and 3CL^{pro} inhibitory activities, five adenosine triazole derivatives **11a**, **11h**, **11i**, **11m**, and

Table 3: ACE2 and 3CL^{pro} inhibitory activity of the selected triazole derivatives.

No	Compounds	IC_{50} value* (μg/mL)	
		ACE2	3CL^{pro}
	Positive control**	80.00 ± 0.04 (nM)	0.033 ± 0.03 (nM)
1	11a	>150	>150
2	11h	>150	>150
3	**11i**	**>150**	**124.80 ± 0.07**
4	**11m**	**142.95 ± 0.22**	**135.62 ± 0.15**
5	11q	>150	>150

*Data represent the mean ± standard deviation of triplicate. *GC376 (Bioscience, US) was employed as a positive control.

11q are selected for these tests. Among the selected compounds, **11a** is a triazole that had anti-inflammatory containing quinazolinone; **11q** is a triazole of ketoprofen with the best activity against RAW 264.7 cells; **11h**, **11i**, and **11m** are compounds containing murrayafoline A and indirubin-3′-oxime scaffolds which are reported to have potential antiviral activities [51, 52]. The results of ACE2 and 3CL^{pro} inhibitory activities of five selected compounds are summarized in Table 3.

Among the five tested triazoles, only two triazoles **11i** and **11m** containing indirubin-3′-oxime moiety exhibited weak inhibitory activity on ACE2 and 3CL^{pro} proteins. The remaining triazoles of ketoprofen and murrayafoline A showed no activity toward both of these proteins. As given results in Table 3, only triazole **11m** displayed weak inhibition of ACE2 protein with an IC_{50} value of 142.95 μg/mL, while conjugates **11i** and **11m** showed 3CL^{pro} inhibitory activity with the IC_{50} values of 124.80 and 135.62 μg/mL. Especially, triazole **11m** containing the 1,2,3-triazole linker at *N1* of indirubin-3′-oxime inhibited both ACE2 and 3CL^{pro} proteins. The ACE2 and 3CL^{pro} inhibitory results of **11i** and **11m** also showed the important role of the 3′-oxime group in activity. The chemical modification of this group in **11i** led to a tendency to lose ACE2 inhibitory activity compared with **11m**. Finally, although indirubin-3′-oxime triazole derivatives with adenosine expressed weak activity compared with the positive controls, these results suggested that indirubin-3′-oxime could also be used as a template for the design of its derivatives for the exploration of anti-SARCoV-2 activity.

3. Conclusion

AZT and 5′-azido adenosine were coupled with various terminal alkynes by the CuAAC reaction to produce 30 novel 1,2,3-triazoles with the full data of structures. Evaluation of the cytotoxic and anti-inflammatory activities and inhibitory effects of ACE2 and 3CL^{pro} proteins showed that adenosine 1,2,3-triazoles were less toxic to HepG2 and LU human carcinoma cell lines. In addition, adenosine1,2,3-triazoles containing the amide group were beneficial for their anti-inflammatory activity. Among them, adenosine 1,2,3-triazoles derived from ketoprofen, an anti-inflammatory drug, showed the strongest inhibitory activity of NO production in LPS-stimulated RAW 264.7 cells with an IC_{50} value of 12.00 μg/mL. In particular, adenosine 1,2,3-triazoles containing the indirubin-3′-oxime scaffold exhibited both inhibitory activities on ACE2 and 3CL^{pro} proteins. Although the activities were not as strong as expected, this was also a valuable suggestion for the use of indirubin-3′-oxime as a template for the design of its new derivatives to prevent the activation of ACE2 and 3CL^{pro} proteins.

4. Experimental

All chemicals were purchased from Sigma Aldrich (118222, Singapore) and used without further purification. Murrayafoline A **8l** was isolated from the roots of *Glycosmis stenocarpa* and demethylated by BBr_3 in CH_2Cl_2 at −78°C to give 1-hydroxy-3-methyl carbazole **8h** according to known procedures described by Cuong et al. [53, 54]. The indirubin-rich powder was obtained by reaction of a water solution of fresh *Strobilanthes cusia* leaves with isatin and converted into indirubin-3′-oxime **8i** using protocols of Lee et al. [55].

^{1}H-NMR and ^{13}C-NMR spectra were recorded at ambient temperature on a Bruker Avance 600 MHz spectrometer (Biospin, Germany) in DMSO-d_6. Chemical shifts δ are quoted in parts per million (ppm) referenced to the residual solvent peak (DMSO at 2.50, 3.32 ppm, and 39.5 ppm) relative to TMS. Mass spectra were recorded by using Agilent LC/MSD Trap SL. Thin-layer chromatography was performed on precoated Silica Gel 60 F_{254} aluminum sheets (Merck, Darmstadt, Germany), and products were visualized under a UV lamp at 254 nm. Column chromatography was carried out on silica gel (40–230 mesh).

4.1. Synthesis of 5′-Azido Adenosine 6. A mixture of 5′-tosyl adenosine (4.21 g, 10.0 mmol) and sodium azide (1.3 mg, 20.0 mmol) in DMF (30 mL) was stirred at 50°C overnight until TLC (CH_2Cl_2:MeOH 4 : 1 v/v) indicated the absence of 5′-tosyl adenosine. The solvent was removed under reduced pressure, and the resulting solid was purified by column chromatography eluted with CH_2Cl_2:MeOH 4 : 1 v/v to give **6**.

Yield (2.35 g, 80%, white solid, m.p. 190–192°C; R_f = 0.42 (CH_2Cl_2/MeOH 15 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.36 (s, 1H, H-8), 8.17 (s, 1H, H-2), 7.28 (s, 2H, 6-NH_2), 5.94 (d, J = 5.4 Hz, 1H, H-1′), 5.57 (d, J = 6.0 Hz, 1H, 3-OH), 5.37 (d, J = 5.4 Hz, 1H, 2′OH), 4.76 (dd, J_1 = 5.4 Hz, J_2 = 6.0 Hz, 1H, H-2′), 4.21 (dd, $J_1 = J_2$ = 5.4 Hz, 1H, H-3), 4.06 (ddd, J_1 = 3.6 Hz, $J_2 = J_3$ = 4.2 Hz, 1H, H-4′), 3.69 (dd, J_1 = 7.2 Hz, J_2 = 13.2 Hz, 1H, H-5a), and 3.57 (dd, J_1 = 3.6 Hz, J_2 = 13.2 Hz, 1H, H-5b); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 165.7 (C-2), 162.1 (C-6), 149.4 (C-4), 139.3 (C-8), 128.7 (C-5), 97.3 (C-1′), 92.4 (C-4′), 82.2 (C-2′), 80.4 (C-3′), and 61.2 (C-5′).

4.2. General Procedure for the Synthesis of O-Propargyl Compounds (Terminal Alkynes 9a–j). To a solution of each 6-hydroxy-2-methyl quinazolinone **8a**–**g** or 4-hydroxyphenyl acetamide **8j** (1 mmol, 1equivalent) in DMF (4 mL), K_2CO_3 (207 mg, 1.5 mmol, 1.5 equivalent) and

propargyl bromide (178 mg, 1.5 mmol, 1.5 equivalent) were added. The mixture was stirred for 24 h at room temperature and poured on cold water, then extracted with EtOAc (3×25 mL), and dried on anhydrous sodium sulfate. The solvent was removed under reduced pressure to give corresponding terminal alkyne crude **9a**–**g** and **9j** that were purified by silica gel column chromatography eluted with *n*-hexane:EtOAc.

4.3. 3-(2-Chlorophenyl)-2-methyl-6-(prop-2-yn-1-yloxy)quinazolin-4(3H)-one (9a). Yield (243.8 mg, 75%), gray powder, m.p. 158–160°C; $R_f = 0.37$ (*n*-hexane/EtOAc 2 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 7.75 (m, 1H, H-6′), 7.68 (m, 1H, H-3′), 7.66 (d, $J = 9.0$ Hz,1H, H-8), 7.61 (d, $J = 3.0$ Hz, H-5), 7.59 (m, 2H. H-4′, H-5′), 7.51 (dd, $J_1 = 3.0$ Hz, $J_2 = 9.0$ Hz, 1H, H-7), 4.95 (d, $J = 2.4$ Hz, 2H, H-1″), 3.61 (t, $J = 2.4$ Hz, 1H, H-3″), 2.09 (s, 3H, 2-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 160.3 (C-4), 155.5 (C-6), 151.5 (C-2), 142.1 (C-10), 135.2 (C-1′), 131.3 (C-2′), 131.1 (C-5′), 130.6 (C-3′), 130.1 (C-4′), 128.7 (C-8), 124.8 (C-7), 120.8 (C-9), 108.0 (C-5), 78.74 (C-2″), 78.68 (C-3″), 56.0 (C-1″), 22.9 (2-CH_3). ESI-HRMS calculated for $C_{18}H_{14}ClN_2O_2$: $[M + H]^+$ (*m*/*z*): 325.0745, found: 325.0738.

4.4. 3-(3-Chlorophenyl)-2-methyl-6-(prop-2-yn-1-yloxy)quinazolin-4(3H)-one (9b). Yield (240.6 mg, 74%), gray powder, m.p. 214–216°C; $R_f = 0.37$ (*n*-hexane/EtOAc 2 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 7.65 (m, 1H, H-2′), 7.63 (d, $J = 9.0$ Hz, 1H, H-8), 7.54 (m, 2H, H-5′, H-6′), 7.58 (d, $J = 3.0$ Hz, 1H, H-5), 7.48 (dd, $J_1 = 3.0$ Hz, $J_2 = 9.0$ Hz, 1H, H-7), 7.44 (m, 1H, H-4′), 4.92 (d, $J = 2.4$ Hz, 2H, H-1″), 3.56 (t, $J = 2.4$ Hz, 1H, H-3″), 2.12 (s, 3H, 2-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 161.2 (C-4), 155.5 (C-6), 152.1 (C-2), 142.7 (C-10), 139.3 (C-3′), 133.8 (C-1′), 131.2 (C-2′), 129.3 (C-5′), 128.8 (C-4′), 128.6 (C-8), 127.6 (C-6′), 124.7 (C-7), 121.1 (C-9), 108.2 (C-5), 78.9 (C-2″), 78.7 (C-3″), 56.1 (C-1″), 23.8 (2-CH_3). ESI-HRMS calculated for $C_{18}H_{14}ClN_2O_2$: $[M + H]^+$ (*m*/*z*): 325.0745, found: 325.0736.

4.5. 3-(2-Fluorophenyl)-2-methyl-6-(prop-2-yn-1-yloxy)quinazolin-4(3H)-one (9c). Yield (225.6 mg, 73%), gray powder, m.p. 151–153°C; $R_f = 0.38$ (*n*-hexane/EtOAc 1 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 7.66 (d, $J = 8.4$ Hz, 1H, H-8), 7.62 (m, 3H, H-6′, H-3′, H-5), 7.50 (m, 2H, H-7, H-5′), 7.42 (m, 1H, H-4′), 4.95 (d, $J = 2.4$ Hz, 2H, H-1″), 3.61 (t, $J = 2.4$ Hz, 1H, H-3″), 2.15 (s, 3H, 2-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 160.4 (C-4), 157.0(d, $J = 246.0$ Hz, C-2′), 155.6 (C-6), 151.8 (C-2), 142.1 (C-10), 131.6 (d, $J = 9$ Hz, C-4′), 130.6 (C-5′), 128.6 (C-8), 125.5 (C-5′), 125.0 (C-7), 124.9 (d, $J = 18.8$ Hz, C-1′), 120.6 (C-9), 116.5 (d, $J = 18.8$ Hz, C-3′), 108.0 (C-5), 78.8 (C-2″, C-3″), 56.0 (C-1″), 23.0 (2-CH_3). ESI-HRMS calculated for $C_{18}H_{14}FN_2O_2$: $[M + H]^+$ (*m*/*z*): 309.1040, found: 309.1034.

4.6. 3-(3-Fluorophenyl)-2-methyl-6-(prop-2-yn-1-yloxy)quinazolin-4(3H)-one (9d). Yield (231.8 mg, 75%), gray powder, m.p. 152–154°C; $R_f = 0.38$ (*n*-hexane/EtOAc 2 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 7.63 (d, $J = 9.0$ Hz, 1H, H-8), 7.62 (m, 1H, H-2′), 7.58 (d, $J = 3.0$ Hz, 1H, H-5), 7.48 (dd, $J_1 = 3.0$ Hz, $J_2 = 9.0$ Hz, 1H, H-7), 7.44 (m, 1H, H-6′), 7.38 (m, 1H, H-5′), 7.31 (m, 1H, H-4′), 4.92 (d, $J = 2.4$ Hz, 2H, H-1″), 3.56 (t, $J = 2.4$ Hz, 1H, H-3″), 2.12 (s, 3H, 3-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 162.4 (d, $J = 243.0$ Hz, C-3′), 161.1 (C-4), 155.5 (C-6), 152.2 (C-2), 142.3 (C-10), 139.5 (d, $J = 9.0$ Hz, C-1), 131.3 (d, $J = 9.0$ Hz, C-5′), 128.6 (C-8), 125.0 (C-6′), 124.8 (C-7), 116.2 (d, $J = 21.0$ Hz, C-4′), 116.2 (d, $J = 21.0$ Hz, C-2′), 108.2 (C-5), 78.9 (C-2″), 78.7 (C-3″), 56.1 (C-1″), 23.7 (2-CH_3). ESI-HRMS calculated for $C_{18}H_{14}FN_2O_2$: $[M + H]^+$ (*m*/*z*): 309.1040, found: 309.1032.

4.7. 3-(4-Fluorophenyl)-2-methyl-6-(prop-2-yn-1-yloxy)quinazolin-4(3H)-one (9e). Yield (222.5 mg, 72%), gray powder, m.p. 154–156°C; $R_f = 0.37$ (*n*-hexane/EtOAc 1 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 7.63 (d, $J = 9.0$ Hz, 1H, H-8), 7.58 (d, $J = 2.7$ Hz, 1H, H-5), 7.51 (m, 2H, H-2′, H-6′), 7.47 (dd, $J_1 = 2.7$ Hz,, $J_2 = 9.0$ Hz, 1H, H-7), 7.40 (m, 2H, H-3′, H-5′), 4.92 (d, $J = 2.4$ Hz, 2H, H-1″), 3.59 (t, $J = 2.4$ Hz, 1H, H-3″), 2.11 (s, 3H, 2-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 162.0 (d, $J = 261.0$ Hz, C-4′), 160.9 (C-4), 155.3 (C-6), 152.4 (C-2), 142.2 (C-10), 134.2 (C-1′), 130.7 (d, $J = 12.0$ Hz, C-2′, C-6′), 128.4 (C-8), 124.5 (C-7), 121.1 (C-9), 116.4 (d, $J = 27.0$ Hz, C-3′, C-5′), 108.5 (C-5), 78.8 (C-2″), 78.7 (C-3″), 55.9 (C-1″), 23.8 (2-CH_3). ESI-HRMS calculated for $C_{18}H_{14}FN_2O_2$: $[M + H]^+$ (*m*/*z*): 309.1040, found: 309.1034.

4.8. 3-(3-Methoxyphenyl)-2-methyl-6-(prop-2-yn-1-yloxy)quinazolin-4(3H)-one (9f). Yield (244.1 mg, 76%), gray powder, m.p. 210–212°C; $R_f = 0.36$ (*n*-hexane/EtOAc 1 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 7.62 (d, $J = 9.0$ Hz, 1H, H-7), 7.58 (d, $J = 3.0$ Hz, 1H, H-5), 7.46 (m, 2H, H-7, H-5′), 7.08 (m, 1H, H-6′), 7.05 (m, 1H, H-2′), 6.97 (m, 1H, H-4′), 4.91 (d, $J = 2.4$ Hz, 2H, H-1″), 3.78 (s, 3H, 3′-OCH_3), 2.13 (s, 3H, 2-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 161.1 (C-4), 160.2 (C-3′), 155.4 (C-6), 152.6 (C-2), 142.3 (C-10), 139.1 (C-1′), 130.4 (C-5′), 128.5 (C-8), 124.7 (C-7), 121.2 (C-9), 120.5 (C-6′) 114.9 (C-4′), 114.2 (C-2′), 108.1 (C-5), 78.9 (C-2″), 78.8 (C-3″), 56.0 (C-1″), 55.5 (3′-OCH_3), 23.6 (2-CH_3). ESI-HRMS calculated for $C_{19}H_{17}N_2O_3$: $[M + H]^+$ (*m*/*z*): 321.1240, found: 321.1234.

4.9. 3-(4-Methoxyphenyl)-2-methyl-6-(prop-2-yn-1-yloxy)quinazolin-4(3H)-one (9g). Yield (234.4 mg, 73%), gray powder, m.p. 209–211°C; $R_f = 0.36$ (*n*-hexane/EtOAc 1 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 7.62 ($J = 8.7$ Hz, 1H, H-8), 7.58 (d, $J = 2.7$ Hz, 1h, H-5), 7.46 (dd, $J_1 = 2.7$ Hz, $J_2 = 8.7$ Hz, 1H, H-7), 7.34 (dd, $J_1 = 2.7$ Hz, $J_2 = 8.7$ Hz, 2H, H-2′, H-6′), 7.04 (dd, $J_1 = 2.7$ Hz, $J_2 = 8.7$ Hz, 2H, H-3′, H-5′), 4.93 (d, $J = 2.4$ Hz, 2H, H-1″), 3.60 (t, $J = 2.4$ Hz, 1H, H-3″), 2.11 (s, 3H, 2-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 161.2 (C-4), 159.2 (C-4′), 155.2 (C-6), 152.8 (C-2), 142.2 (C-10), 130.4 (C-1′), 129.4 (C-2′, C-6′), 128.3 (C-8), 124.4 (C-7), 121.1 (C-9), 108.0 (C-5), 78.8 (C-2″), 78.6 (C-

3″), 55.9 (C-1″), 55.4 (4′-OCH_3, 2-CH_3). ESI-HRMS calculated for $C_{19}H_{17}N_2O_3$: $[M+H]^+$ (*m*/*z*): 321.1240, found: 321.1231.

4.10. 2-(4-(Prop-2-ynyloxy)phenyl)acetamide (9j). Yield (156.8 mg, 83%), while powder, m.p. 167–169°C; $R_f = 0.4$ (*n*-hexane/acetone 1 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 7.39 (s, 1H, -$CONH_{2a}$), 7.19 (ddd, $J_1 = 2.4$ Hz, $J_2 = 5.4$ Hz, $J_3 = 9.6$ Hz, 2H, H-3, H-5), 6.91 (ddd, $J_1 = 2.4$ Hz, $J_2 = 5.4$ Hz, $J_3 = 9.6$ Hz, H-2, H-6), 6.81 (s, 1H, -$CONH_{2b}$), 4.76 (d, $J = 2.4$ Hz, 2H, H-1′), 3.52 (t, $J = 2.4$ Hz, 1H, H-3′), 3.31 (s, 2H, 4-CH_2-); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 172.5 (C-7), 155.8 (C-1), 130.0 (C-3, C-5), 129.2 (C-4), 114.6 (C-2, C-6), 79.4 (C-2′), 78.0 (C-3′), 55.3 (C-1′), 41.3 (4-CH_2-). ESI-HRMS calculated for $C_{18}H_{15}N_2O_2$: $[M+H]^+$ (*m*/*z*): 190.0868, found:190.0854.

5. 10-(Prop-2-ynyl)acridin-9(10H)-one (9k)

5.1. 1-Methoxy-3-methyl-9-(prop-2-ynyl)-9H-carbazole (9l). The synthesis of **9h, 9k, 9l,** and **9n** was described in our previous report [45].

The synthesis of **9i** and **9m** was also described in our previous study [46].

*5.2. General Procedure for the Synthesis of Amide **9o**–**q**.* Each acid (3,4,5-trimethoxybenzoic acid **8o,** 4-methoxyphenyl acetic acid **8p,** or ketoprofen **8q** (1.0 mmol, 1 equivalent)) was dissolved in anhydrous DMF at −20°C, followed by addition of EDC (193 mg), propargyl amine (0.08 mL, 1,2 equivalent), triethylamine (0.16 mL), and DMAP (126 mg). The mixture was stirred at room temperature overnight, and the solvent was then removed under reduced pressure to give crude products that were purified by silica gel column chromatography eluted with *n*-hexane:acetone to yield corresponding amide **9o**–**q**.

5.3. 3,4,5-Trimethoxy-N-(prop-2-yn-1-yl)benzamide (9o). Yield (142.6 mg, 57%), white powder, m.p. 172–174°C; $R_f = 0.37$ (*n*-hexane/acetone 2 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.86 (t, $J = 5.4$ Hz, 1H, -CONH-), 7.20 (s, 2H, H-2, H-6), 4.06 (m, 2H, H-1′), 3.83 (s, 6H, 3-OCH_3, 5-OCH_3), 3.70 (s, 3H, 4-OCH_3), 3.12 (t, $J = 2.4$ Hz, 1H, H-3′); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 165.3 (C-7), 152.6 (C-3, C-5), 140.1 (C-4), 128.9 (C-1), 104.8 (C-2, C-6), 81.3 (C-2′), 72.8 (C-3′), 60.0 (4-OCH_3), 56.0 (3-OCH_3, 5-OCH_3), 28.5 (C-1′). ESI-HRMS calculated for $C_{13}H_{16}NO_4$: $[M+H]^+$ (*m*/*z*): 250.1080, found: 250.1071.

5.4. 2-(4-Methoxyphenyl)-N-(prop-2-yn-1-yl)acetamide (9p). Yield (110.2 mg, 54%), white powder, m.p. 112–114°C; $R_f = 0.39$ (*n*-hexane/acetone 2 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.39 (s, brd, 1H, -CONNH-), 7.16 (dd, $J_1 = 2.1$ Hz, $J_2 = 6.9$ Hz, 2H, H-3, H-5), 6.85 (dd, $J_1 = 2.1$ Hz, $J_2 = 6.9$ Hz, 2H, H-2, H-6), 3,84 (dd,, $J_1 = 2.4$ Hz, $J_2 = 5.4$ Hz, 2H, H-1′), 3.72 (s, 3H, 4-OCH_3), 3.31 (s, 2H, 1-CH_2-), 3.08 (t, d, $J = 2.4$ Hz, 1H, H-3′). ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 170.1 (-CONH-), 157.9 (C-4), 129.9 (C-3, C-5), 127.9 (C-1), 113.6 (C-2, C-6), 81.1 (C-2′), 72.9 (C-3′), 55.0 (4-OCH_3), 41.1 (1-CH_2-), 27.9 (C-1′). ESI-HRMS calculated for $C_{12}H_{14}NO_2$: $[M+H]^+$ (*m*/*z*): 204.1025, found: 204.0982.

5.5. 2-(3-Benzoylphenyl)-N-(prop-2-yn-1-yl)propanamide (9q). Yield (163.6 mg, 56%), white powder, m.p. 137–139°C; $R_f = 0.4$ (*n*-hexane/acetone 1 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.48 (t, $J = 5.4$ Hz, 1H, -CONH-), 7.83 (m, 3H, H-3′, H-7′, H-5), 7.69 (t, $J = 7.5$ Hz, 1H, H-5′), 7.60 (m, 4H, H-4′, H-6′, H-7, H-9), 7.50 (t, $J = 7.5$ Hz, 1H, H-8), 3.84 (m, 2H, H-1″), 3.72 (m, 1H, H-2), 3.07 (t, $J = 2.4$ Hz, 1H, H-3″), 1.36 (d, $J = 7.2$ Hz, 3H, H-3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 195.7 (C-1′), 172.6 (C-1), 142.3 (C-4), 137.0 (C-2′), 136.9 (C-6), 132.6 (C-5□), 131.6 (C-9), 129.6 (C-3′, C-7′), 128.54 (C-5, C-8), 128.46 (C-6′), 128.1 (C-7), 80.9 (C-2″), 73.0 (C-3″), 44.6 (C-2), 28.0 (C-1″), 18.2 (C-3). ESI-HRMS calculated for $C_{19}H_{18}NO_2$: $[M+H]^+$ (*m*/*z*): 292.1338, found: 292.1330.

6. General Procedure for the Synthesis of AZT and Adenosine Triazole Derivatives

A suspension of each terminal alkyne (1mmol) and AZT **1** or 5′-azido adenosine (1 mmol) in 4 mL of acetonitrile:H_2O (1 : 1, v/v) was stirred for 30 min; then, 1M solution of $CuSO_4$ 1M solution (0.5 mL) was added. The reaction mixture was stirred vigorously, followed by addition of four drops of hydrazine hydrate. After TLC indicated the absence of the starting materials, the solvent was removed under reduced pressure. The resulting solid was stirred with 1M EDTA solution (10 mL) for 30 min and left overnight, then filtered and washed thoroughly with water, and dried in a vacuum desiccator to yield the corresponding crude triazoles that were purified by column chromatography/silica gel eluted with CH_2Cl_2:MeOH to give **10a**–**m** and **11a**–**q**.

*6.1. 1-(4-(4-(((3-(2-Chlorophenyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1H,3H)-dione (**10a**).* Yield (307.9 mg, 52%), white powder, m.p. 160–162°C; $R_f = 0.41$ (CH_2Cl_2/MeOH 15 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 11.34 (s, 1H, H-3), 8.45 (s, 1H, H-5″), 7.82 (d, $J = 1.2$ Hz, 1H, H-6), 7.75 (m,1H, H-6‴), 7.68 (m, 3H, H-8‴, H-3‴, H-5‴), 7.59 (m, 2H, H-4‴, H-5‴), 7.54 (dd, $J_1 = 2.7$ Hz, $J_2 = 8.7$ Hz, 1H, H-7‴), 6.43 (t, $J = 6.6$ Hz, 1H, H-1′), 5.40 (m, 1H, H-3′), 5.30 (m, 3H, 4″-CH_2-, 5′-OH), 4.25 (m, 1H, H-4′), 3.72 (m, 1H, H-5′a), 3.64 (m, 1H, H-5′b), 2.76 (m, 1H, H-2′a), 2.65 (m, 1H, H-2′b), 2.09 (s, 3H, 2‴-CH_3), 1.81 (d, $J = 1.2$ Hz, 3H, 5-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 163.7 (C-4), 160.3 (C-4‴), 156.5 (C-6‴), 151.5 (C-2‴), 150.5 (C-2), 142.6 (C-10‴), 142.0 (C-4″), 136.2 (C-6), 135.3 (C-1‴′), 131.3 (C-2‴′), 131.2 (C-5‴′), 130.7 (C-3‴′), 130.2 (C-4‴′), 128.8 (C-8‴), 128.6 (C-6‴′), 124.7 (C-7‴), 124.4 (C-5″), 120.9 (C-9‴), 109.7 (C-5), 107.9 (C-5‴), 84.5 (C-1′), 83.9 (C-4′), 61.7 (4″-CH_2-), 60.8 (C-5′), 59.3 (C-3′), 37.2 (C-2′), 23.0 (2‴-CH_3), 12.2 (5-CH_3). ESI-HRMS calculated for $C_{28}H_{27}ClN_7O_6$: $[M+H]^+$ (*m*/*z*): 592.1712, found: 592.1708.

6.2. 1-(4-(4-(((3-(3-Chlorophenyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1H,3H)-dione ***(10b)***. Yield (296.1 mg, 50%), white powder, m.p. 164–166°C; $R_f = 0.41$ (CH_2Cl_2/MeOH 15 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 11.34 (s,1H, H-3), 8.44 (s,1H, H-5″), 7.81 (d, $J = 1.2$ Hz, 1H, H-6), 7.67 (s, 1H, H-5‴), 7.65 (d, $J = 3.0$ Hz, 1H, H-2‴′), 7.63 (d, $J = 8.7$ Hz, 1H, H-8‴), 7.60 (m, 2H, H-5‴″, H-6‴″), 6.42 (t, $J = 6.6$ Hz, 1H, H-1′), 5.40 (m, 1H, H-3′), 5.30 (m, 3H, 4″-CH_2-, 5′-OH), 4.24 (m, 1H, H-4′), 3.71 (m, 1H, H-5′a), 3.64 (m, 1H, H-5′b), 2.75 (m, 1H, H-2′a), 2.66 (m, 1H, H-2′b), 2.12 (s, 3H, 3‴-CH_3), 1.81 (d, $J = 1.2$ Hz, 3H, 5-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 163.8 (C-4), 161.1 (C-4‴), 156.3 (C-6‴), 151.8 (C-2‴), 150.5 (C-2), 142.6 (C-4″), 142.0 (C-10‴), 139.3 (C-3‴′), 136.3 (C-6), 133.7 (C-1‴″), 131.1 (C-2‴″), 129.2 (C-5‴″), 128.7 (C-4‴″), 128.5 (C-8‴), 127.5 (C-6‴″), 124.4 (C-5″), 124.4 (C-7‴), 121.1 (C-9‴), 109.7 (C-5), 107.8 (C-5‴), 84.5 (C-1′), 83.9 (C-4′), 61.7 (4″-CH_2-), 60.8 (C-5′), 59.4 (C-3′), 37.2 (C-2′), 23.7 (2‴-CH_3), 12.3 (5-CH_3). ESI-HRMS calculated for $C_{28}H_{27}ClN_7O_6$: $[M + H]^+$ (m/z): 592.1712, found: 592.1710.

6.3. 1-(4-(4-(((3-(2-Florophenyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1H,3H)-dione ***(10c)***. Yield (305.4 mg, 53%), white powder, m.p. 150–152°C; $R_f = 0.4$ (CH_2Cl_2/MeOH 15 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 11.35 (s, 1H, H-3), 8.46 (s, 1H, H-5″), 7.82 (d, $J = 1.2$ Hz, 1H, H-6), 7.70 (d, $J = 2.4$ Hz, 1H, H-5‴), 7.66 (d, $J = 8.4$ Hz, 1H, H-8‴), 7.63 (m, 2H, H-3‴″, H-6‴″), 7.55 (dd, $J_1 = 2.4$ Hz, $J_2 = 8.4$ Hz,1H, H-7‴), 7.51 (dt, $J_1 = 2.4$ Hz, $J_2 = 8.4$ Hz, 1H, H-5‴″), 7.43 (dt, $J_1 = 2.4$ Hz, $J_2 = 8.4$ Hz, 1H, H-4‴″), 5.77 (t, $J = 6.6$ Hz, 1H, H-1′), 5.41 (m, 1H, H-3′), 5.30 (m, 2H, 5′-OH, 4″-CH_2), 4.25 (m, 1H, H-4′), 3.71 (m, 1H, H-5′a), 3.65 (m, 1H, H-5′b), 2.76 (m, 1H, H-2′a), 2.69 (m, 1H, H-2′b), 2.16 (s, 3H, 2‴-CH_3), 1.82 (d, $J = 1.2$ Hz, 3H, 5-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 163.8 (C-4), 160.5 (C-4‴), 157.1 (d, $J = 246.0$ Hz, C-2‴″), 156.6 (C-6‴), 151.7 (C-2‴), 150.5 (C-3‴), 142.6 (C-10‴), 141.9 (C-4″), 136.3 (C-6), 131.7 (d, $J = 7.5$ Hz, C-6‴), 130.7 (C-4‴″), 128.6 (C-8‴), 125.6 (C-5‴″), 125.1 (d, $J = 17.3$ Hz, C-1‴″), 124.7 (C-7‴), 124.4 (C-5″), 120.7 (C-9‴), 116.6 (d, $J = 17.3$ Hz, C-3‴″), 109.7 (C-5), 107.9 (C-5‴), 84.5 (C-1′), 83.9 (C-4′), 61.7 (4″-CH_2-), 60.8 (C-5′), 59.4 (C-3′), 37.2 (C-2′), 23.1 (2‴-CH_3), 12.3 (5-CH_3). ESI-HRMS calculated for $C_{28}H_{27}FN_7O_6$: $[M + H]^+$ (m/z): 576.2008, found: 576.2001.

6.4. 1-(4-(4-(((3-(3-Florophenyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1H,3H)-dione ***(10d)***. Yield (299.6 mg, 52%), white powder, m.p. 152–154°C; $R_f = 0.4$ (CH_2Cl_2/MeOH 5 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 11.34 (s,1H, H-3), 8.45 (s,1H, H-5″), 7.81 (d, $J = 1.2$ Hz, 1H, H-6), 7.66 (d, $J = 3.0$ Hz, 1H, H-5‴), 7.63 (d, $J = 9.0$ Hz, 1H, H-8‴), 7.61 (m, 1H, H-2‴″), 7,52 (dd, $J_1 = 3.0$ Hz, $J_2 = 9.0$ Hz, 1H, H-7‴), 7.46 (m, 1H, H-6‴″), 7.39 (m, 1H, H-5‴″), 7.33 (m, 1H, H-4‴″), 6.42 (t, $J = 6.6$ Hz, 1H, H-1′), 5.40 (m, 1H, H-3′), 5.29 (m, 3H, 4″-CH_2-, 5′-OH), 4.24 (m, 1H, H-4′), 3.71 (m, 1H, H-5′a), 3.63 (m, 1H, H-5′b), 2.75 (m, 1H, H-2′a), 2.66 (m, 1H, H-2′b), 2.13 (s, 3H, 3‴-CH_3), 1.81 (d, $J = 1.2$ Hz, 3H, 5-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 163.7 (C-4), 162.2 (d, $J = 243.0$ Hz, C-3‴″), 161.0 (C-4‴), 156.3 (C-6‴), 151.8 (C-2‴), 150.4 (C-2), 142.6 (C-4″), 142.0 (C-10‴), 139.5 (d, $J = 10.5$ Hz, C-1‴″), 136.2 (C-6), 133.7 (C-1‴″), 131.2 (d, $J = 10.5$ Hz, C-5‴″), 128.5 (C-8‴), 125.0 (C-7‴), 124.4 (d, $J = 3.0$ Hz, C-6‴″), 121.2 (C-9‴), 116.2 (m, C-2‴″, C-4‴″), 109.6 (C-5), 107.8 (C-5‴), 84.4 (C-1′), 83.9 (C-4′), 61.6 (4″-CH_2-), 60.8 (C-5′), 59.3 (C-3′), 37.2 (C-2′), 23.6 (2‴-CH_3), 12.2 (5-CH_3). ESI-HRMS calculated for $C_{28}H_{27}FN_7O_6$: $[M + H]^+$ (m/z): 576.2008, found: 576.2001.

6.5. 1-(4-(4-(((3-(4-Florophenyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1H,3H)-dione ***(10e)***. Yield (288.1 mg, 50%), white powder, m.p. 159–161°C; $R_f = 0.4$ (CH_2Cl_2/MeOH 15 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 11.33 (s, 1H, H-3), 8.44 (s, 1H, H-5″), 7.81 (d, $J = 1.2$ Hz, 1H, H-6), 7.65 (d, $J = 3.0$ Hz, 1H, H-5‴), 7.63 (d, $J = 9.0$ Hz, 1H, H-8‴), 7.51 (m, 3H, H-2‴″, H-6‴″, H-7‴), 7.40 (m, 2H, H-3‴″, H-5‴″), 6.42 (t, $J = 6.6$ Hz, 1H, H-1′), 5.40 (m, 1H, H-3′), 5.28 (m, 3H, 4″-CH_2-, 5′-OH), 4.24 (m, 1H, H-4′), 3.71 (m, 1H, H-5′a), 3.63 (m, 1H, H-5′b), 2.75 (m, 1H, H-2′a), 2.66 (m, 1H, H-2′b), 2.11 (s, 3H, 2‴-CH_3), 1.81 (s, 3H, 5-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 163.7 (C-4), 161.8 (d, $J = 260.0$ Hz, C-4‴″), 161.2 (C-4‴), 156.3 (C-6‴), 152.2 (C-2‴), 150.4 (C-2), 142.6 (C-10‴), 142.0 (C-4″), 136.2 (C-6), 134.2 (C-1‴″), 130.7 (d, $J = 10.5$ Hz, C-2‴″, C-6‴″), 128.4 (C-8‴), 124.4 (C-7‴), 121.2 (C-9‴), 116.4 (d, $J = 27.0$ Hz, C-3‴″, C-5‴″), 109.6 (C-5), 107.8 (C-5‴), 84.4 (C-1′), 83.9 (C-4′), 61.6 (4″-CH_2-), 60.8 (C-5′), 59.3 (C-3′), 37.1 (C-2′), 23.8 (2‴-CH_3), 12.2 (5-CH_3). ESI-HRMS calculated for $C_{28}H_{27}FN_7O_6$: $[M + H]^+$ (m/z): 576.2008, found: 576.2001.

6.6. 1-(4-(4-(((3-(3-Methoxyphenyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1H,3H)-dione ***(10f)***. Yield (317.6 mg, 54%), white powder, m.p. 184–186°C; $R_f = 0.39$ (CH_2Cl_2/MeOH 15 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 11.34 (s, 1H, H-3), 8.44 (s, 1H, H-5″), 7.81 (d, $J = 1.2$ Hz, 1H, H-6), 7.66 (d, $J = 1.8$ Hz, 1H, H-5‴), 7.62 (d, $J = 8.4$ Hz, 1H, H-8‴), 7.51 (dd, $J_1 = 1.8$ Hz, $J_2 = 8.4$ Hz, 1H, H-7‴), 7.47 (t, $J = 8.4$ Hz, 1H, H-5‴″), 7.08 (m, 2H, H-2‴″, H-6‴″), 6.99 (dd, $J_1 = 1.8$ Hz, $J_2 = 8.4$ Hz, 1H, H-4‴″), 6.42 (t, $J = 6.6$ Hz, 1H, H-1′), 5.40 (m, 1H, H-3′), 5.29 (m, 3H, 4″-CH_2-, 5′-OH), 4.24 (m, 1H, H-4′), 3.79 (s, 3H, 3‴″-OCH_3), 3.71 (m, 1H, H-5′a), 3.63 (m, 1H, H-5′b), 2.75 (m, 1H, H-2′a), 2.66 (m, 1H, H-2′b), 2.14 (s, 3H, 2‴-CH_3), 1.81 (d, $J = 1.2$ Hz, 3H, 5-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 163.8 (C-4), 161.0 (C-4‴), 160.1 (C-3‴″), 156.3 (C-6‴), 152.2 (C-2‴), 150.5 (C-2), 142.6 (C-10‴), 142.1 (C-4″), 139.1 (C-1‴″), 136.3 (C-6), 130.3 (C-5‴″), 128.4 (C-8‴), 124.4 (C-7‴), 124.3 (C-5″),

121.2 (C-6‴), 120.4 (C-9‴), 114.7 (C-4‴), 114.1 (C-2‴), 109.7 (C-5), 107.8 (C-5‴), 84.5 (C-1′), 83.9 (C-4′), 61.6 (4″-CH_2-), 60.8 (C-5′), 59.4 (C-3′), 55.4 (3‴-OCH_3), 37.2 (C-2′), 23.6 (2‴ -CH_3), 12.2 (5-CH_3). ESI-HRMS calculated for $C_{29}H_{30}N_7O_7$: $[M+H]^+$ (*m*/*z*): 588.2287, found: 588.2202.

6.7. 1-(4-(4-(((3-(4-Methoxyphenyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1H,3H)-dione ***(10g)****.* Yield (300.1 mg, 51%), white powder, m.p. 185–187°C; $R_f = 0.39$ (CH_2Cl_2/MeOH 15 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 11.34 (s, 1H, H-3), 8.44 (s, 1H, H-5″), 7.81 (s, 1H, H-6), 7.65 (d, $J = 3.0$ Hz, 1H, H-5‴), 7.61 (d, $J = 8.7$ Hz, 1H, H-8‴), 7.50 (dd, $J_1 = 3.0$ Hz, $J_2 = 8.7$ Hz, 1H, H-7‴), 7.33 (dd, $J_1 = 3.0$ Hz, $J_2 = 8.7$ Hz, 2H, H-2‴, H-6‴), 7.10 (d, $J = 8.7$ Hz, 2H, H-3‴, H-5‴), 6.42 (t, $J = 6.6$ Hz, 1H, H-1′), 5.40 (m, 1H, H-3′), 5.29 (m, 3H, 4″-CH_2-, 5′-OH), 4.24 (m, 1H, H-4′), 3.83 (s, 3H, 4‴-OCH_3), 3.71 (m, 1H, H-5′a), 3.63 (m, 1H, H-5′b), 2.75 (m, 1H, H-2′a), 2.66 (m, 1H, H-2′b), 2.11 (s, 3H, 2‴-CH_3), 1.81 (s, 3H, 5-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 163.7 (C-4), 161.3 (C-4‴), 159.3 (C-4‴), 156.2 (C-6‴), 152.8 (C-2‴), 150.4 (C-2), 142.6 (C-10‴), 142.1 (C-4″), 136.2 (C-6), 130.5 (C-1‴), 129.5 (C-2‴, C-6‴), 128.4 (C-8‴), 124.4 (C-7‴), 124.3 (C-5″), 121.2 (C-9‴), 114.7 (C-3‴, C-5‴), 109.6 (C-5), 107.8 (C-5‴), 84.4 (C-1′), 83.9 (C-4′), 61.6 (4″-CH_2-), 60.8 (C-5′), 59.3 (C-3′), 55.4 (4‴-OCH_3), 37.2 (C-2′), 23.8 (2‴ -CH_3), 12.2 (5-CH_3). ESI-HRMS calculated for $C_{29}H_{30}N_7O_7$: $[M+H]^+$ (*m*/*z*): 588.2287, found: 588.2201.

6.8. 1-(5-(Hydroxymethyl)-4-(4-(((3-methyl-9H-carbazol-1-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1H,3H)-dione ***(10h)****.* Yield (264.2 mg, 49%), white powder, m.p. 188–190°C; $R_f = 0.42$ (CH_2Cl_2/MeOH 15 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 11.35 (s, 1H, H-3), 11.04 (s, 1H, H-9‴), 8.53 (s, 1H, H-5″), 8.00 (d, $J = 7.8$ Hz, 1H, H-5‴), 7.83 (d, $J = 1.2$ Hz, 1H, H-6), 7.51 (s, 1H, H-4‴), 7.45 (d, $J = 7.8$ Hz, 1H, H-8‴), 7.32 (dt, $J_1 = 1.2$ Hz, $J_2 = 8.1$ Hz, 1H, H-7‴), 7.07 (t, $J = 7.8$ Hz, 1H, H-6‴), 7.03 (s, 1H, H-2‴), 6.45 (t, $J = 6.6$ Hz, 1H, H-1′), 5.43 (m, 1H, H-3′), 5.36 (s, 2H, N_9‴ -CH_2-), 5.31 (t, $J = 5.1$ Hz, 1H, 5′-OH), 4.28 (m, 1H, H-4′), 3.74 (m, 1H, H-5′a), 3.66 (m, 1H, H-5′b), 2.77 (m, 1H, H-2′a), 2.70 (m, 1H, H-2′b), 2.50 (s, 3H, 3‴-CH_3), 1.82 (s, 3H, 5-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 163.7 (C-4), 150.4 (C-2), 144.1 (C-1‴), 143.2 (C-4″), 139.8 (C-13‴), 136.2 (C-6), 128.0 (C-3‴), 127.9 (C-10‴), 125.1 (C-7‴), 124.4 (C-12‴), 123.7 (C-5″), 122.4 (C-11‴), 120.0 (C-6‴), 118.3 (C-8‴), 112.7 (C-4‴), 111.3 (C-2‴), 109.6 (C-5), 109.1 (C-5‴), 84.5 (C-1′), 84.0 (C-4′), 61.5 (4″-CH_2-), 60.8 (C-5′), 59.3 (C-3′), 37.2 (C-2′), 12.2 (5-CH_3). ESI-HRMS calculated for $C_{26}H_{26}N_6O_5$: $[M+H]^+$ (*m*/*z*): 539.1863, found: 539.2014.

6.9. 1-(5-(Hydroxymethyl)-4-(4-((((((2Z,3E)-2′-oxo-[2,3′-biindolinylidene]-3-ylidene)amino)oxy)methyl)-1H-1,2,3-triazol-1-yl)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1H,3H)-dione ***(10i)****.* Yield (256.6 mg, 44%), red powder, m.p. 230–232°C; $R_f = 0.4$ (CH_2Cl_2/MeOH 15 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 11.66 (H-1‴), 11.33 (s, 1H, H-3), 10.74 (H-1‴), 8.53 (d, $J = 7.2$ Hz, 1H, H-4‴), 8.52 (s, 1H, H-5″), 8.13 (d, $J = 7.2$ Hz, 1H, H-4‴), 7.80 (d, $J = 0.9$ Hz, 1H, H-6), 7.42 (m, 2H, H-6‴, H-7‴), 7.15 (dt, $J_1 = 1.2$ Hz, $J_2 = 7.2$ Hz 1H, H-6‴), 7.02 (m, 2H, H-5‴, H-5‴), 6.89 (d, $J = 7.2$ Hz, 1H, H-7‴), 6.44 (t, $J = 6.9$ Hz, 1H, H-1′), 5.72 (s, 2H, 4″-CH_2-), 5.42 (m, 1H, H-3′), 5.26 (t, $J = 5.1$ Hz, 1H, 5′-OH), 4.22 (m, 1H, H-4′), 3.67 (m, 1H, H-5′a), 3.60 (m, 1H, H-5′b), 2.73 (m, 1H, H-2′a), 2.63 (m, 1H, H-2′b), 1.81 (d, $J = 0.9$ Hz, 3H, 5-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 170.8 (C-2‴), 163.7 (C-4), 151.8 (C-3‴), 150.4 (C-2), 145.6 (C-2‴), 143.5 (C-7‴a), 143.0 (C-4″), 138.7 (C-7‴a), 136.2 (C-6), 133.0 (C-6‴), 128.5 (C-4‴), 126.4 (C-6‴), 124.5 (C-5″), 123.6 (C-4‴), 122.1 (C-3‴a), 121.4 (C-5‴), 120.7 (C-5‴), 116.1 (C-3‴a), 111.7 (C-7‴), 109.6 (C-5), 108.8 (C-7‴), 100.5 (C-3‴), 84.4 (C-4′), 83.9 (C-1′), 69.2 (4″-CH_2), 60.7 (C-5′), 59.3 (C-3′), 37.1 (C-2′), 12.2 (5-CH_3). ESI-HRMS calculated for $C_{29}H_{27}N_8O_6$: $[M+H]^+$ (*m*/*z*): 583.2054, found: 588.2048.

6.10. 2-(4-((1-(2-(Hydroxymethyl)-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)tetrahydrofuran-3-yl)-1H-1,2,3-triazol-4-yl)methoxy)phenyl)acetamide (10j). Yield (300.9 mg, 66%), white powder, m.p. 261–263°C; $R_f = 0.4$ (CH_2Cl_2/MeOH 9 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.41 (s, 1H, H-5″), 7.82 (s, 1H, H-6), 7.38 (s, 1H, -$CONH_{2a}$), 7,19 (d, $J = 8.4$ Hz, 2H, H-3‴, H-5‴), 6.79 (d, $J = 8.4$ Hz, 2H, H-2‴, H-6‴), 6.81 (s, 1H, -$CONH_{2b}$), 6.43 (t, $J = 6.6$ Hz, 1H, H-1′), 5.39 (m, 1H, H-4′), 5.27 (t, $J = 5.1$ Hz, 1H, 5′-OH), 5.13 (s, 2H, 4″-CH_2-), 4.24 (m, 1H, H-3′), 3.71 (m, 1H, H-5′a), 3.64 (m, 1H, H-5′b), 3.29 (s, 2H, 4‴-CH_2-), 2.75 (m, 1H, H-2a), 2.67 (m, 1H, H-2b), 1.82 (s, 3H, 5-CH_3). ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 172.5 (-$CONH_2$), 163.7 (C-4), 156.6 (C-1‴), 150.4 (C-2), 143.1 (C-4″), 136.2 (C-6), 130.1 (C-3‴, C-5‴), 128.9 (C-4‴), 124.1 (C-5″), 114.4 (C-2‴, C-6‴), 109.6 (C-5), 84.4 (C-4′), 83.9 (C-1′), 61.1 (4″-CH_2-), 60.7 (C-5′), 59.3 (C-5′), 41.3 (4‴-CH_2-), 37.1 (C-2′), 12.2 (5-CH_3). ESI-HRMS calculated for $C_{21}H_{25}N_6O_6$: $[M+H]^+$ (*m*/*z*): 457.1835, found: 457.1821.

6.11. 1-(5-(Hydroxymethyl)-4-(4-((9-oxoacridin-10(9H)-yl)methyl)-1H-1,2,3-triazol-1-yl)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1H,3H)-dione (10k). Yield (235.2 mg, 47%), pale yellow powder, m.p. 279–281°C; $R_f = 0.45$ (CH_2Cl_2/MeOH 15 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)):11.31 (s, 1H, H-3), 8.37 (dd, $J_1 = 1.5$ Hz, $J_2 = 7.8$ Hz, 2H, H-1‴, H-8‴), 8.32 (s, 1H, H-5″), 7.95 (d, $J_2 = 7.8$ Hz, 2H, H-4‴, H-5‴), 7.83 (m, 2H, H-3‴, H-6‴), 7.77 (d, $J = 1.2$ Hz, 1H, H-6), 7.36 (t, $J = 7.8$ Hz, 2H, H-2‴, H-7‴), 6,39 (t, 6.9. 1-(5-(Hydroxymethyl)-4-(4-(((((2Z,3E)-2′-oxo-[2,3′-biindolinylidene]-3-$J = 6.6$ Hz, 1H, H-1′), 5.82 (s, 2H, 4″-CH_2-), 5.33 (m, 1H, H-3′), 5.21 (t, $J = 5.1$ Hz, 1H, 5′-OH), 4.18 (dd, $J_1 = 3.9$ Hz, $J_2 = 8.7$ Hz, 1H, H-4′), 3.66 (m, 1H, H-5′a), 3.57 (m, 1H, H-5′b), 2.68 (m, 1H,H-2′a), 2.59 (m, 1H, H-2′), 1.79 (d, $J = 1.2$ Hz, 3H, 5-CH_3). ^{13}C-NMR (150 MHz, DMSO-d_6, δ

(ppm)): 176.6 (C-9‴), 163.6 (C-4), 150.4 (C-2), 142.8 (C-4″), 141.8 (C-11‴, C-14‴), 136.1 (C-6), 134.2 (C-3‴,C-6‴), 126.6 (C-1‴, C-8‴), 123.1 (C-5″), 121.7 (C-12‴, C-13‴), 121.5 (C-2‴, C-7‴), 116.2 (C-4‴, C-5‴), 109.6 (C-5), 84.3 (C-4′), 83.8 (C-1′), 60.7 (C-5′), 59.3 (C-3′), 41.7 (4″-CH_2-), 37.1 (C-2′), 12.2 (5-CH_3). ESI-HRMS calculated for $C_{26}H_{25}N_6O_5$: $[M+H]^+$ (m/z): 501.1886, found: 501.1865.

*6.12. 1-(5-(Hydroxymethyl)-4-(4-((1-methoxy-3-methyl-9H-carbazol-9-yl)methyl)-1H-1,2,3-triazol-1-yl)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1H,3H)-dione (**10l**).* Yield (261.7 mg, 52%), white powder, m.p. 208–210°C; $R_f = 0.42$ (CH_2Cl_2/MeOH 15 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 11.34 (s, 1H, H-3), 8.03 (d, $J = 7.8$ Hz, 1H, H-5‴), 8.00 (s, 1H, H-5″), 7.75 (d, $J = 1.2$ Hz, 1H, H-6), 7.69 (d, $J = 7.8$ Hz, 1H, H-8‴), 7.51 (s, 1H, H-4‴), 7.41 (dt, $J_1 = 1.2$ Hz, $J_2 = 7.8$ Hz, 1H, H-7‴), 7.15 (t, $J = 7.8$ Hz, 1H, H-6‴), 6.89 (s, 1H, H-2‴), 6.37 (t, $J = 6.3$ Hz, 1H, H-1′), 5.86 (s, 2H, $N_{9‴}$-CH_2-), 5.27 (m, 1H, H-3′), 5.21 (s, 1H, 5′-OH), 4.13 (m, 1H, H-4′), 3.98 (s, 3H, 1‴-OCH_3), 3.63 (d, $J = 12.0$ Hz, 1H, H-5′a), 3.54 (d, $J = 12.0$ Hz, 1H, H-5′b), 2.62 (m, 1H, H-2′a), 2.54 (m, 1H, H-2′b), 2.45 (s, 3H, 3‴-CH_3), 1.78 (d, $J = 0.6$ Hz, 3H, 5-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 163.8 (C-4), 150.4 (C-2), 146.38 (C-1‴), 144.8 (C-4″), 140.4 (C-13‴), 136.2 (C-6), 129.1 (C-3‴), 127.1 (C-10‴), 125.6 (C-7‴), 124.2 (C-12‴), 122.7 (C-5″), 122.5 (C-11‴), 120.1 (C-6‴), 119.0 (C-8‴), 11.5 (C-4‴), 110.0 (C-2‴), 109.6 (C-5′), 109.5 (C-5‴), 84.4 (C-1′), 83.9 (C-4′), 60.8 (C-5′), 59.2 (C-3′), 55.9 (1‴-OCH_3), 37.2 (C-2′), 21.3 (3‴ -CH_3), 12.2 (5-CH_3). ESI-HRMS calculated for $C_{26}H_{27}N_6O_5$: $[M+H]^+$ (m/z): 503.2044, found: 503.2032.

*6.13. 1-(4-(4-(((2Z,3E)-3-(Hydroxyimino)-2′-oxo-[2,3′-biindolinylidene]-1′-yl)methyl)-1H-1,2,3-triazol-1-yl)-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1H,3H)-dione (**10m**).* Overall yield (261.9 mg, 44%), red powder, m.p. 260–262°C; $R_f = 0.4$ (CH_2Cl_2/MeOH 7 : 1 v/v). ESI-HRMS calculated for $C_{29}H_{27}N_8O_6$: $[M+H]^+$ (m/z): 583.2053, found: 583.2048.

*6.14. 1-(4-(4-(((2Z,3E)-3-(Hydroxyimino)-2′-oxo-[2,3′-biindolinylidene]-1′-yl)methyl)-1H-1,2,3-triazol-1-yl)-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1H,3H)-dione (**10m1**).* ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 11.66 (s, 1H, H-oxime), 11.32 (s, 1H, H-3), 10.73 (s, 1H, H-1‴′), 8.53 (m, 2H, H-4‴, H-5‴), 8.14 (d, $J = 7.8$ Hz, 1H, H-4‴′), 7.80 (s, 1H, H-6), 7.42 (m, 2H, H-6‴′, H-7‴′), 7.15 (m, 1H, H-6‴), 7.01 (m, 2H, H-5‴, H-5‴′), 6.88 (m, 1H, H-7‴), 6.45 (t, $J = 6.6$ Hz, 1H, H-1′), 5.72 (s, 2H, 4″-CH_2-), 5.35 (m, 1H, H-4′), 5.25 (t, $J = 5.4$ Hz, 1H, 5′-OH), 4.22 (m, 1H, H-3′), 3.68 (m, 1H, 5′-CH_{2a}-), 3.60 (m, 1H, 5′-CH_{2b}-), 2.72 (m, 1H, H-2′a), 2.65 (m, 1H, H-2′b), 1.80 (s, 3H, 5-CH_3). ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 170.8 (C-2‴), 163.6 (C-4), 151.8 (C-3‴′), 150.38 (C-2), 147.1 (C-2‴′), 145.57 (C-7‴′a), 143.5 (C-4″), 138.6 (C-7‴a), 136.1 (C-6), 132.9 (C-6‴′), 128.4 (C-4‴′′), 126.4 (C-6‴), 124.5 (C-5″), 123.6 (C-4‴), 122.0 (C-3‴a), 121.3 (C-5‴), 120.7 (C-5‴′), 116.1 (C-3‴′a), 111.7 (C-7‴′), 109.5 (C-5), 108.8 (C-7‴), 100.5 (C-3‴), 84.5 (C-4′), 83.9 (C-1′), 69.2 (4″-CH_2-), 61.4 (C-5′), 59.3 (C-3′), 37.1 (C-2′), 12.16 (5-CH_3).

*6.15. 1-(4-(5-(((2Z,3E)-3-(Hydroxyimino)-2′-oxo-[2,3′-biindolinylidene]-1′-yl)methyl)-1H-1,2,3-triazol-1-yl)-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1H,3H)-dione (**10m2**-Isomer).* ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 11.66 (s, 1H, H-oxime), 11.34 (s, 1H, H-3), 10.73 (s, 1H, H-1‴′), 8.52 (s, 1H, H-4″), 8.46 (d, $J = 7.8$ Hz, 1H, H-4‴), 8.17 (d, $J = 7.8$ Hz, 1H, H-4‴′), 7.83 (s, 1H, H-6), 7.42 (m, 2H, H-6‴′, H-7‴′), 7.15 (m, 1H, H-6‴), 7.01 (m, 2H, H-5‴, H-5‴′), 6.88 (m, 1H, H-7‴), 6.51 (t, $J = 6.6$ Hz, 1H, H-1′), 5.68 (s, 2H, 4″-CH_2-), 5.42 (m, 1H, H-4′), 5.25 (t, $J = 5.4$ Hz, 1H, 5′-OH), 4.28 (m, 1H, H-3′), 3.68 (m, 1H, 5′-CH_{2a}-), 3.60 (m, 1H, 5′-CH_{2b}-), 2.72 (m, 1H, H-2′a), 2.65 (m, 1H, H-2′b), 1.80 (s, 3H, 5-CH_3). ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 170.8 (C-2‴), 163.6 (C-4), 151.9 (C-3‴′), 150.36 (C-2), 147.1 (C-2‴′), 145.60 (C-7‴′a), 143.3 (C-5″), 138.6 (C-7‴a), 136.0 (C-6), 133.0 (C-6‴′), 128.5 (C-4‴′′), 126.5 (C-6‴), 124.5 (C-4″), 123.6 (C-4‴), 122.1 (C-3‴a), 121.3 (C-5‴), 120.9 (C-5‴′), 116.1 (C-3‴′a), 111.7 (C-7‴′), 109.6 (C-5), 108.8 (C-7‴), 100.6 (C-3‴), 84.8 (C-4′), 84.4 (C-1′), 69.5 (4″-CH_2-), 60.9 (C-5′), 60.7 (C-3′), 37.1 (C-2′), 12.21 (5-CH_3).

6.16. 6-((1-((5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1H-1,2,3-triazol-4-yl)methoxy)-3-(2-chlorophenyl)-2-methylquinazolin-4(3H)-one (11a). Yield (253.1 mg, 41%), white powder, m.p. 200–202°C; $R_f = 0.37$ (CH_2Cl_2/MeOH 6 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.27 (d, $J = 2.7$ Hz, 1H, H-8), 8.17 (s, 1H, H-2), 8.11 (s, 1H, H-5″), 7.75 (m, 1H, H-3‴′), 7.67 (m, 2H, H-6‴′, H-5‴), 7.64 (d, $J = 8.7$ Hz, 1H, H-8‴), 7.58 (m, 2H, H-4‴′, H-5‴′), 7.51 (dd, $J_1 = 2.7$ Hz, $J_2 = 8.7$ Hz, 1H, H-7‴), 7.29 (s, 2H, 6-NH_2), 5.93 (d, $J = 5.4$ Hz, 1H, H-1′), 5.60 (d, $J = 6.0$ Hz, 1H, 3′-OH), 5.49 (d, $J = 5.4$ Hz, 1H, 2′-OH), 5.21 (m, 2H, 4″-CH_2-), 4.81 (m, 2H, H-5′), 4.67 (m, 1H, H-2′), 4.30 (m, 2H, H-3′, H-4′); ^{13}C-NMR (150 MHz, DMSO-d_6, 25°C, TMS, δ (ppm)): 160.3 (C-4‴), 156.5 (C-6‴), 156.1 (C-2‴), 152.7 (C-2), 151.4 (C-6), 149.3 (C-4), 142.2 (C-10‴), 141.9 (C-4″), 139.9 (C-8), 135.2 (C-1‴′), 131.3 (C-5‴′), 131.1 (C-2‴′), 130.7 (C-6‴′), 128.8 (C-4‴′), 128.6 (C-8‴), 125.4 (C-5″), 124.7 (C-7‴), 120.9 (C-9‴), 119.3 (C-5), 107.8 (C-5‴), 87.8 (C-1′), 82.4 (C-4′), 72.6 (C-2′), 71.0 (C-3′), 61.6 (4″-CH_2-), 51.5 (C-5′), 22.9 (2‴-CH_3). ESI-HRMS calculated for $C_{28}H_{26}ClN_{10}O_5$: $[M+H]^+$ (m/z): 617.1777, found: 617.1771.

6.17. 6-((1-((5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1H-1,2,3-triazol-4-yl)methoxy)-3-(3-chlorophenyl)-2-methylquinazolin-4(3H)-one (11b). Yield (265.4 mg, 43%), white powder, m.p. 184–186°C; $R_f = 0.37$ (CH_2Cl_2/MeOH 6 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.26 (s, 1H, H-8), 8.16 (s, 1H, H-2), 8.09

(s, 1H, H-5″), 7.66 (s, 1H, H-2‴″), 7.63 (d, J = 3.0 Hz, 1H, H-5‴), 7.60 (m, 3H, H-8‴, H-6‴″, H-5‴″), 7.48 (dd, J_1 = 3.0 Hz, J_2 = 9.0 Hz, 1H, H-7‴), 7.45 (m, 1H, H-4‴″), 7.27 (s, 2H, 6-NH_2), 5.91 (d, J = 5.4 Hz, 1H, H-1′), 5.59 (d, J = 6.0 Hz, 1H, 3′-OH), 5.45 (d, J = 5.4 Hz, 1H, 2′-OH), 5.21 (d, J = 12.0 Hz, 1H, 4″-CH_{2a}-), 5.18 (d, J = 12.0 Hz, 1H, 4″-CH_{2b}-), 4.79 (m, 2H, H-5′), 4.66 (m, 1H, H-2′), 4.29 (m, 2H, H-3′, H-4′); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 161.0 (C-4‴), 156.3 (C-6‴), 156.1 (C-2‴), 152.7 (C-2), 151.7 (C-6), 144.3 (C-4), 142.2 (C-10‴), 141.9 (C-4″), 139.9 (C-8), 139.3 (C-3‴″), 133.6 (C-1‴″), 131.1 (C-2‴″), 129.1 (C-5‴″), 128.7 (C-6‴″), 128.4 (C-8‴), 127.5 (C-4‴″), 125.4 (C-5″), 124.4 (C-7‴), 121.1 (C-9‴), 107.8 (C-5‴), 87.8 (C-1′), 82.3 (C-4′), 72.6 (C-2′), 70.9 (C-3′), 61.5 (4″-CH_2-), 51.4 (C-5′), 23.7 (2‴-CH_3). ESI-HRMS calculated for $C_{28}H_{26}ClN_{10}O_5$: $[M + H]^+$ (m/z): 617.1777, found: 617.1745.

6.18. 6-((1-((5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1H-1,2,3-triazol-4-yl)methoxy)-3-(2-fluorophenyl)-2-methylquinazolin-4(3H)-one (11c). Yield (268.0 mg, 43%), white powder, m.p. 179–181°C; R_f = 0.38 (CH_2Cl_2/MeOH 6 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.27 (s, 1H, H-8), 8.16 (s, 1H, H-2), 8.11 (s, 1H, H-5″), 7.63 (m, 4H, H-5‴, H-8‴, H-3‴″, H-6‴″), 7.51 (m, 2H, H-7‴, H-4‴″), 7.42 (t, J = 7.5 Hz, 1H, H-5‴″), 7.30 (s, 2H, 6-NH_2), 5.91 (d, J = 5.4 Hz, 1H, H-1′), 5.61 (d, J = 6.0 Hz, 1H, 3′-OH), 5.60 (d, J = 4.8 Hz, 1H, 2′-OH), 5.20 (m, 2H, 4″-CH_2-), 4.79 (m, 2H, H-5′), 4.66 (m, 1H, H-2′), 4.29 (m, 2H, H-3′, H-4′), 2.15 (s, 3H, 2‴-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 160.5 (C-4‴), 157.0 (d, J = 246.0 Hz, C-2‴″), 156.6 (C-6‴), 156.1 (C-2‴), 152.7 (C-2), 151.6 (C-6), 149.3 (C-4), 142.2 (C-10‴), 141.8 (C-4″), 139.9 (C-8), 131.6 (d, J = 7.5 Hz, C-4‴″), 131.4 (d, J = 7.5 Hz, C-6‴), 130.7 (C-3‴″), 128.6 (C-8‴), 125.5 (C-5‴″), 125.4 (C-5″), 125.0 (d, J = 16.0 Hz, C-1‴″), 120.7 (C-9‴), 107 (C-5‴), 87.8 (C-1′), 82.4 (C-4′), 72.6 (C-2′), 71.0 (C-3′), 61.5 (4″-CH_2-), 51.5 (C-5′), 23.1 (2‴-CH_3). ESI-HRMS calculated for $C_{28}H_{25}FN_{10}O_5Na$: $[M+Na]^+$ (m/z): 623.1891, found: 623.1886.

*6.19. 6-((1-((5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1H-1,2,3-triazol-4-yl)methoxy)-3-(3-fluorophenyl)-2-methylquinazolin-4(3H)-one (**11d**).* Yield (264.5 mg, 44%), white powder, m.p. 176–78°C; R_f = 0.38 (CH_2Cl_2/MeOH 6 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.26 (s, 1H, H-8), 8.16 (s, 1H, H-2), 8.10 (s, 1H, H-5″), 7.62 (m, 3H, H-8‴, H-5‴″), 7.49 (dd, J_1 = 3.0 Hz, J_2 = 9.0 Hz, 1H, H-7‴), 7.46 (ddd, J_1 = J_2 = 2.4 Hz, J_3 = 9.6 Hz, H-4‴″), 7.39 (m, 1H, H-2‴″), 7.32 (m, 1H, H-6‴″), 7.28 (s, 2H, 6-NH_2), 5.91 (d, J = 5.4 Hz, 1H, H-1′), 5.60 (d, J = 12.0 Hz, 1H, 4″-CH_{2a}-), 5.18 (d, J = 12.0 Hz, 1H, 4″-CH_{2b}-), 4.79 (m, 2H, H-5′), 4.66 (dd, J_1 = J_2 = 6.0 Hz, 1H, H-2′), 4.28 (m, 2H, H-3′, H-4′), 2.12 (s, 3H, 2‴-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 162.3 (d, J = 243 Hz, C-3‴″), 161.0 (C-4‴), 156.3 (C-6‴), 156.1 (C-2‴), 152.7 (C-2), 151.7 (C-6), 149.3 (C-4), 142.2 (C-10‴), 141.9 (C-4″), 139.9 (C-8), 131.1 (d, J = 10.5 Hz, C-1‴″), 131.1 (d, J = 10.5 Hz, C-5‴″), 128.4 (C-8‴), 125.4 (C-5″), 124.9 (C-6‴″), 124.4 (C-7‴), 121.1 (C-9‴), 119.1 (C-5), 116.2 (d, J = 16.5 Hz, C-4‴″), 116.0 (d, J = 16.5 Hz, C-2‴″), 107.7 (C-5‴), 87.8 (C-1′), 82.3 (C-4′), 72.5 (C-2′), 70.9 (C-3′), 61.5 (4″-CH_2-), 51.4 (C-5′), 23.6 (2‴-CH_3). ESI-HRMS calculated for $C_{28}H_{26}FN_{10}O_5$: $[M + H]^+$ (m/z): 601.2072, found: 601.2066.

*6.20. 6-((1-((5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1H-1,2,3-triazol-4-yl)methoxy)-3-(4-fluorophenyl)-2-methylquinazolin-4(3H)-one (**11e**).* Yield (261.7 mg, 42%), white powder, m.p. 199–201°C; R_f = 0.38 (CH_2Cl_2/MeOH 6 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.26 (s, 1H, H-8), 8.16 (s, 1H, H-2), 8.10 (s, 1H, H-5″), 7.63 (d, J = 3.0 Hz, 1H, H-5‴), 7.60 (d, J = 8.4 Hz, 1H, H-8‴), 7.52 (m, 2H, H-2‴″, H-6‴″), 7.48 (dd, J_1 = 3.0 Hz, J_2 = 8.4 Hz, 1H, H-7‴), 7.40 (dt, J_1 = 1.8 Hz, J_2 = 8.4 Hz, 2H, H-3‴″, H-5‴″), 7.28 (s, 2H, 6-NH_2), 5.91 (d, J = 5.4 Hz, H-1′), 5.60 (d, J = 6.0 Hz, 1H, 3′-OH), 5.49 (d, J = 4.8 Hz, 1H, 2′-OH), 5.21 (d, J = 12.0 Hz, 1H, 4″-CH_{2a}-), 5.18 (d, J = 12.0 Hz, 1H, 4″-CH_{2b}-), 4.79 (m, 2H, H-5′), 4.66 (dd, J_1 = J_2 = 5.4 Hz, 1H, H-2′), 4.29 (m, 2H, H-3′, H-4′), 2.11 (s, 3H, 2‴-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 162.0 (d, J = 261 Hz, C-4‴″), 161.1 (C-4‴), 156.3 (C-6‴), 156.1 (C-2‴), 152.7 (C-2), 152.2 (C-6), 149.3 (C-4), 142.2 (C-10‴), 142.0 (C-4″), 139.9 (C-8), 134.2 (C-1‴″), 130.7 (d, J = 9.0 Hz, C-2‴″, C-6‴″), 128.4 (C-8‴), 125.4 (C-5″), 124.3 (C-7‴), 121.1 (C-10‴), 119.2 (C-5), 116.5 (d, J = 22.5 Hz, C-3‴″, C-5‴″), 107.8 (C-5‴), 87.8 (C-1′), 82.4 (C-4′), 72.6 (C-2′), 70.9 (C-3′), 61.5 (4″-CH_2-), 51.5 (C-5′), 23.8 (2‴-CH_3). ESI-HRMS calculated for $C_{28}H_{25}FN_{10}O_5Na$: $[M+Na]^+$ (m/z): 623.1891, found: 623.1886.

6.21. 6-((1-((5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1H-1,2,3-triazol-4-yl)methoxy)-3-(3-methoxyphenyl)-2-methylquinazolin-4(3H)-one (11f). Yield (257.6 mg, 42%), white powder, m.p. 180–182°C; R_f = 0.36 (CH_2Cl_2/MeOH 6 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.27 (s, 1H, H-8), 8.17 (s, 1H, H-2), 8.10 (s, 1H, H-5″), 7.63 (d, J = 3.0 Hz, 1H, H-5‴), 7.61 (d, J = 8.4 Hz, 1H, H-8‴), 7.48 (m, 2H, H-7‴, H-5‴″), 7.30 (s, 2H, 6-NH_2), 7.08 (m, 2H, H-3‴″, H-2‴″), 6.99 (m, 1H, H-6‴″), 5.92 (d, J = 5.4 Hz, 1H, H-1′), 5.61 (d, J = 6.0 Hz, 1H, 3′-OH), 5.50 (d, J = 5.4 Hz, 1H, 2′-OH), 5.21 (d, J = 12.0 Hz, 1H, 4″-CH_{2a}-), 5.18 (d, J = 12.0 Hz, 1H, 4″-CH_{2b}-), 4.79 (m, 2H, H-5′), 4.61 (dd, J_1 = 6.0 Hz, J_2 = 6.0 Hz, 1H, H-2″), 4.30 (m, 2H, H-3′, H-4′), 3.80 (s, 3H, 3‴″-OCH_3), 2.11 (2‴-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 161.0 (C-4‴), 160.1 (C-3‴″), 156.3 (C-6‴), 156.1 (C-2‴), 152.7 (C-2), 152.1 (C-6), 149.3 (C-4), 142.3 (C-10‴), 142.0 (C-4″), 139.9 (C-8), 139.1 (C-1‴″), 130.3 (C-5‴″), 128.4 (C-8‴), 125.4 (C-5″), 124.3 (C-7‴), 121.2 (C-9‴), 120.4 (C-6‴″), 119.3 (C-5), 114.7 (C-4‴″), 114.1 (C-2‴″), 107.7 (C-5‴), 87.8 (C-1′), 82.4 (C-4′), 72.6

(C-2′), 71.0 (C-3′), 61.5 (4″-CH_2-), 55.4 (3‴′-OCH_3), 51.5 (C-5′), 23.6 (2‴-CH_3). ESI-HRMS calculated for $C_{29}H_{29}N_{10}O_5$: $[M+H]^+$ (m/z): 613.2193, found: 613.2267.

6.22. 6-((1-((5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1H-1,2,3-triazol-4-yl)methoxy)-3-(4-methoxyphenyl)-2-methylquinazolin-4(3H)-one (11g). Yield (273.1 mg, 43%), white powder, m.p. 181–183°C; $R_f = 0.36$ (CH_2Cl_2/MeOH 6 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.26 (s, 1H, H-8), 8.16 (s, 1H, H-2), 8.10 (s, 1H, H-5″), 7.63 (d, $J = 2.7$ Hz, 1H, H-5‴), 7.60 (d, $J = 9.0$ Hz, 1H, H-8‴), 7.47 (dd, $J_1 = 2.7$ Hz, $J_2 = 9.0$ Hz, 1H, H-7‴), 7.34 (dd, $J_1 = 2.7$ Hz, $J_2 = 9.0$ Hz, 2H, H-2‴′, H-6‴′), 7.29 (s, 2H, 6-NH_2), 7.09 (dd, $J_1 = 2.7$ Hz, $J_2 = 9.0$ Hz, 2H, H-3‴′, H-5‴′), 5.92 (d, $J = 5.4$ Hz, 1H, H-1′), 5.61 (d, $J = 6.0$ Hz, 1H, 3′-OH), 5.49 (d, $J = 5.4$ Hz, 1H, 2′-OH), 5.21 (d, $J = 12.0$ Hz, 1H, 4″-CH_{2a}-), 5.17 (d, $J = 12.0$ Hz, 1H, 4″-CH_{2b}-), 4.80 (m, 2H, H-5′), 4.66 (dd, $J_1 = J_2 = 5.4$ Hz, 1H, H-2′), 4.29 (m, 2H, H-3′, H-4′), 3.84 (s, 3H, 4‴′-OCH_3), 2.11 (s, 3H, 2‴-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 161.3 (C-4‴), 159.2 (C-4‴′), 156.2 (C-6‴), 156.1 (C-2‴), 152.7 (C-2), 149.3 (C-4), 142.2 (C-10‴), 142.0 (C-4″), 139.9 (C-8), 130.5 (C-1‴′), 129.5 (C-2‴′, C-6‴′), 128.3 (C-8‴), 125.4 (C-5″), 124.3 (C-7‴), 121.2 (C-9‴), 119.2 (C-5), 114.7 (C-3‴′, C-5‴′), 107.7 (C-5‴), 87.8 (C-1′), 82.3 (C-4′), 72.6 (C-2′), 70.9 (C-3′), 61.5 (4″-CH_2-), 55.4 (4′-OCH_3), 51.4 (C-5′), 23.8 (2‴-CH_3). ESI-HRMS calculated for $C_{29}H_{28}N_{10}O_5Na$: $[M+Na]^+$ (m/z): 635.2091, found: 635.2084.

*6.23. 2-(6-Amino-9H-purin-9-yl)-5-((4-(((3-methyl-9H-carbazol-1-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)tetrahydrofuran-3,4-diol (**11h**).* Yield (211.3 mg, 40%), white powder, m.p. 186–188°C; $R_f = 0.41$ (CH_2Cl_2/MeOH 6 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 11.01 (s, 1H, N_9‴-H), 8.30 (s, 1H, H-8), 8.20 (s, 1H, H-3), 8.17 (s, 1H, H-5″), 7.99 (d, $J = 7.8$ Hz, 1H, H-5‴), 7.48 (s, 1H, H-4‴), 7.42 (d, $J = 7.8$ Hz, 1H, H-8‴), 7.30 (m, 3H, H-7, 6-NH_2), 7.09 (t, $J = 7.8$ Hz, 1H, H-6‴), 6.98 (s, 1H, H-2‴), 5.93 (d, $J = 5.4$ Hz, 1H, H-7′), 5.62 (d, $J = 6.0$ Hz, 1H, 3′-OH), 5.49 (d, $J = 3.6$ Hz, 1H, 2′-OH), 5.28 (d, $J = 12.0$ Hz, 1H, 4″ -CH_{2a}-), 5.25 (d, $J = 12.0$ Hz, 1H, 4″-CH_{2b}-), 4.82 (m, 2H, H-5′), 4.73 (m, 1H, H-2′), 4.32 (m, 2H, H-4′, H-3′), 2.45 (s, 3H, 3‴-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 156.1 (C-6), 152.6 (C-2), 149.2 (C-4), 144.0 (C-1‴), 142.7 (C-4″), 139.9 (C-8), 139.8 (C-13‴), 127.9 (C-3‴), 127.8 (C-10‴), 125.3 (C-7‴), 125.0 (C-12‴), 123.6 (C-5″), 122.3 (C-11‴), 120.0 (C-6‴), 119.2 (C-5), 118.2 (C-8‴), 112.5 (C-4‴), 111.3 (C-2‴), 109.0 (C-5‴), 87.9 (C-1′), 82.3 (C-4′), 72.6 (C-2′), 71.0 (C-3′), 61.3 (4″-CH_2-), 31.6 (C-5□), 21.5 (3‴-CH_3-). ESI-HRMS calculated for $C_{26}H_{26}N_9O_4$: $[M+H]^+$ (m/z): 528.2109, found: 482.2108.

6.24. (2Z,3E)-3-(((1-((5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1H-1,2,3-triazol-4-yl)methoxy)imino)-[2,3′-biindolinylidene]-2′-one (11i). Yield (218.9 mg, 36%), red powder, m.p. 203–205°C; $R_f = 0.37$ (CH_2Cl_2/MeOH 6 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.68 (d, $J = 7.8$ Hz, 1H, H-4‴′), 8.25 (s, 1H, H-8), 8.23 (d, $J = 7.8$ Hz, 1H, H-4‴), 8.16 (s, 1H, H-2), 7.90 (s, 1H, H-5″), 7.41 (m, 2H, H-6‴, H-7‴), 7.29 (s, 2H, 6-NH_2), 7.13 (m, 1H, H-6‴′), 7.07 (d, $J = 7.8$ Hz, 1H, H-7‴′), 7.04 (m, 1H, H-5‴), 6.83 (m, 1H, H-5‴′), 5.89 (d, $J = 5.4$ Hz, 1H, H-1′), 5.57 (d, $J = 5.4$ Hz, 1H, 3′-OH), 5.43 (d, $J = 7.2$ Hz, 1H, 2′-OH), 5.09 (d, $J = 15.6$ Hz, 1H, 4″-CH_{2a}), 5.04 (d, $J = 15.6$ Hz, 1H, 4″-CH2b), 4.71 (m, 2H, H-5′), 4.65 (m, 1H, H-2′), 4.23 (m, 2H, H-3′, H-4′); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 168.6 (C-2‴′), 156.1 (C-3‴), 152.7 (C-2), 151.3 (C-6), 149.3 (C-4), 145.8 (C-2‴), 144.7 (C-7‴a), 142.6 (C-4″), 139.9 (C-8), 138.3 (C-7‴′a), 132.1 (C-6‴), 127.9 (C-4‴), 125.8 (C-6‴′), 124.0 (C-5″), 122.8 (C-4‴′), 121.93 (C-3‴′a), 121.70 (C-5‴′), 121.02 (C-5‴), 119.26 (C-5), 116.50 (C-3‴a), 111.6 (C-7‴), 108.2 (C-7‴′), 97.7 (C-3‴′), 87.9 (C-1′), 82.3 (C-4′), 72.1 (C-2′), 70.9 (C-3′), 51.4(C-5′), 34.4 (N-O-CH_2-). ESI-HRMS calculated for $C_{29}H_{26}N_{11}O_5$: $[M+H]^+$ (m/z): 608.2119, found: 608.2106.

*6.25. 2-(4-((1-((5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1H-1,2,3-triazol-4-yl)methoxy)phenyl)acetamide (**11j**).* Yield (202.5 mg, 42%), white powder, m.p. 189–191°C; $R_f = 0.36$ (CH_2Cl_2/MeOH 6 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.27 (s, 1H, H-8), 8.16 (s, 1H, H-2), 8.06 (s, 1H, H-5″), 7.37 (s, 1H, -$CONH_{2a}$), 7.30 (s, 2H, 6-NH_2), 7.16 (d, $J = 8.4$ Hz, 2H, H-3‴, H-5‴), 6.93 (m, 2H, H-2‴, H-6‴), 6.80 (s, 1H, -$CONH_{2b}$), 5.92 (d, $J = 5.4$ Hz, 1H, H-1′), 5.61 (s, brd, 1H, 3′-OH), 5.50 (s, brd, 1H, 2′ -OH), 5.06 (d, $J = 11.7$ Hz, 1H, 4″-CH_{2a}-), 5.02 (d, $J = 11.7$ Hz, 1H, 4″-CH_{2b}-), 4.77 (m, 2H, H-5′), 4.67 (s, brd, 1H, H-2′), 4.29 (m, 2H, H-3′, H-4′), 3.29 (s, 2H, 4‴-CH_2-); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 172.5 ($CONH_2$), 156.6 (C-6), 156.1 (C-1‴), 152.7 (C-2), 149.3 (C-4), 142.7 (C-4″), 139.9 (C-8), 130.0 (C-3‴, C-5‴), 128.8 (C-5″), 125.1 (C-4‴), 119.2 (C-5), 114.3 (C-2‴, C-6‴), 87.8 (C-1′), 82.3 (C-4′), 72.5 (C-2′), 70.9 (C-3′), 60.9 (4″-CH_2-), 51.4 (C-5′), 41.3 (4‴-CH_2-). ESI-HRMS calculated for $C_{21}H_{24}N_9O_5$: $[M+H]^+$ (m/z): 482.1901, found: 482.1894.

*6.26. 10-((1-((5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl)acridin-9(10H)-one (**11k**).* Yield (226.3 mg, 43%), pale yellow powder, m.p. 217–219°C; $R_f = 0.39$ (CH_2Cl_2/MeOH 6 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.34 (dd, $J_1 = 1.8$ Hz, $J_2 = 7.8$ Hz, 2H, H-1‴, H-8‴), 8.26 (s, 1H, H-8), 8.17 (s, 1H, H-2), 8.00 (s, 1H, H-5″), 7.84 (d, $J = 7.8$ Hz, 2H, H-4‴, H-5‴), 7.75 (dt, $J_1 = 1.8$ Hz, $J_2 = 7.8$ Hz, 2H, H-3‴, H-6‴), 7.43 (s, 2H, 6-NH_2), 7.32 (t, $J = 7.8$ Hz, 2H, H-2‴, H-7‴), 5.90 (d, $J = 4.8$ Hz, 1H, H-1′), 5.74 (d, $J = 18$ Hz, 1H, 4″-CH_{2a}-), 5.69 (d, $J = 18$ Hz, 1H, 4″-CH_{2b}-), 5.63 (s, 1H, 3′-OH), 5.49 (s, 1H, 2′-OH), 4.73 (d, $J = 5.4$ Hz, 2H, 5′-CH_2-), 4.69 (m, 1H, H-2′), 4.25 (m, 2H, H-3′, H-4′); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 176.6 (C-9‴), 156.0 (C-6), 152.5 (C-2), 149.2 (C-4), 142.3 (C-4″), 141.7 (C-11‴, C-14‴), 140.0 (C-8), 134.1 (C-3‴, C-6‴), 126.6 (C-1‴, C-8‴), 124.2 (C-5″), 121.7 (C-12‴, C-13‴), 121.5 (C-2‴, C-7‴),

119.3 (C-5), 116.2 (C-4‴, C-5‴), 87.9 (C-1′), 82.2 (C- 4′), 72.6 (C-2′), 70.9 (C-3′), 51.4 (C-5′), 48.6 (4″-CH_2-). ESI-HRMS calculated for $C_{26}H_{24}N_9O_4$: $[M+H]^+$ (m/z): 526.1952, found: 526.1925.

*6.27. 2-(6-Amino-9H-purin-9-yl)-5-((4-((1-methoxy-3-methyl-9H-carbazol-9-yl)methyl)-1H-1,2,3-triazol-1-yl)methyl) tetrahydrofuran-3,4-diol (**11l**).* Yield (215.7 mg, 40%), white powder, m.p. 192–194°C; $R_f = 0.41$ (CH_2Cl_2/MeOH 6 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.25 (s, 1H, H-8), 8.14 (s, 1H, H-2), 7.99 (d, $J = 7.8$ Hz, 1H, H-5‴), 7.63 (s, 1H, H-5′), 7.62 (d, $J = 7.8$ Hz, 1H, H-8‴), 7.47 (s, 1H, H-4‴), 7.36 (m, 1H, H-7‴), 7.32 (s, 2H, 6-NH_2), 7.12 (dd, $J_1 = 0.6$ Hz, $J_2 = 7.8$ Hz, 1H, H-6‴), 6.79 (d, $J = 0.6$ Hz, 1H, H-2‴), 5.86 (d, $J = 5.4$ Hz, 1H, H-1′), 5.76 (d, $J = 15.6$ Hz, 1H, 4″ -CH_{2a}-), 5.72 (d, $J = 15.6$ Hz, 1H, 4″-CH_{2b}-), 5.61 (s, brd, 1H, 3′ -OH), 5.47 (s, brd, 1H, 2′ -OH), 4.69 (m, 1H, H-2′), 4.65 (m, 2H, H-5′), 4.17 (m, 2H, H-4′, H-3′), 3.81 (s, 3H, 1‴-OCH_3), 2.44 (s, 3H, 3‴-CH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 156.1 (C-6), 152.6 (C-2), 149.2 (C-4), 146.2 (C-1‴), 144.2 (C-4″), 140.3 (C-13‴), 139.9 (C-8), 128.9 (C-3‴), 126.9 (C-10‴), 125.4 (C-7‴), 124.1 (C-12‴), 123.6 (C-5″), 122.3 (C-11‴), 119.9 (C-6‴), 119.3 (C-8‴), 118.8 (C-5), 112.4 (C-4‴), 109.9 (C-2‴), 109.3 (C-5‴), 87.8 (C-1′), 82.4 (C-4′), 72.4 (C-2′), 70.9 (C-3′), 55.5 (4″-CH_2-, 1‴-OCH_3), 51.2 (C-5′), 21.3 (3‴-CH_3). ESI-HRMS calculated for $C_{27}H_{28}N_6O_5Na$: $[M+Na]^+$ (m/z): 539.2019, found: 539.2013.

6.28. (2Z,3E)-1′-((1-((5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl)-3-(hydroxyimino)-[2,3′-biindolinylidene]-2′-one (11m). Yield (231.1 mg, 38%), red powder, m.p. 215–217°C; $R_f = 0.36$ (CH_2Cl_2/MeOH 6 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 11.64 (s, 1H, H-oxime), 10.73 (s,1H, H-1‴″), 8.52 (d, $J = 7.5$ HZ, 1H, H-4‴), 8.27 (s, 1H, H-8), 8.19 (s, 1H, H-2), 8.16 (s, 1H, H-5□□), 8.05 (d, $J = 7.5$ Hz, 1H, H-4‴″), 7.40 (m, 2H, H-6‴″, H-7‴″), 7.29 (s, 2H, 6-NH_2), 7.11 (dt, $J_1 = 1.2$ Hz, $J_2 = 7.5$ Hz, 1H, H-6′‴), 6.95 (m, 2H, H-5‴, H-5‴″), 6.87 (d, $J = 7.5$ Hz, 1H, H-7′‴), 5.92 (d, $J = 5.4$ Hz, 1H, H-1′), 5.64 (d, $J = 18.6$ Hz, 1H, 1′‴-CH_{2a}), 5.59 (m, 2H, 1′‴-CH2b, 3′-OH), 5.47 (d, $J = 5.4$ Hz, 1H, 2′-OH), 4.81 (m, 2H, H-5′), 4.68 (m, 1H, H-4′), 4.29 (m, 2H, H-2′, H-3′); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 170.8 (C-2′‴), 156.1 (C-3‴″), 152.6 (C-2), 151.7 (C-6), 149.22 (C-4), 145.5 (C-2‴″), 143.53 (C-7‴″a), 142.5 (C-4″), 139.9 (C-8), 138.6 (C-7′‴a), 132.9 (C-6‴″), 128.4 (C-4‴″), 126.4 (C-6′‴), 125.5 (C-5″), 123.6 (C-4′‴), 122.1 (C-3′‴a), 121.3 (C-5′‴), 120.7 (C-5‴″), 119.2 (C-5), 116.1 (C-3‴″a), 111.7 (C-7‴″), 108.8 (C-7′‴), 100.5 (C-3′‴), 87.9 (C-1′), 82.3 (C-4′), 72.6 (C-2′), 70.9 (C-3′), 69.1 (-N_1-CH_2-), 51.5 (C-5′). ESI-HRMS calculated for $C_{29}H_{26}N_{11}O_5$: $[M+H]^+$ (m/z): 608.2119, found: 608.2109.

*6.29. N-((1-((5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl)-2-(9-oxoacridin-10(9H)-yl)acetamide (**11n**).* Yield (233.3 mg, 40%), pale yellow powder, m.p. 201–203°C; $R_f = 0.37$ (CH_2Cl_2/MeOH 5 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.89 (t, $J = 5.4$ Hz, 1H, CONH), 8.33 (dd, $J_1 = 1.5$ Hz, $J_2 = 8.1$ Hz, 2H, H-1′‴, H-8′‴), 8.29 (s, 1H, H-8), 8.18 (s, 1H, H-2), 7.85 (s, 1H, H-5″), 7.72 (m, 2H, H-3′‴, H-6′‴), 7.57 (d, $J = 8.1$ Hz, 2H, H-4′‴, H-5′‴), 7.31 (m, 4H, H-2′‴, H-7′‴, 6-NH_2), 5.95 (d, $J = 5.4$ Hz, 1H, H-1′), 5.60 (s, brd, 1H, 3′-OH), 5.52 (s, brd, 1H, 2′-OH), 5.18 (s, 2H, 10′‴-CH_2-), 4.76 (m, 2H, 4″-CH_2-), 4.67 (m, 1H, H-2′), 4.36 (d, $J = 5.4$ Hz, 2H, H-5′), 4.28 (m, 2H, H-3′, H-4′); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 176.7 (C-9′‴), 167.1 (CONH), 156.1 (C-6), 152.7 (C-2), 149.3 (C-4), 144.4 (C-11′‴, C-14′‴), 142.4 (C-4′‴), 139.8 (C-8), 133.9 (C-3‴′, C-6‴′), 126.4(C-1‴′, C-8‴′), 123.4 (C-5″), 121.6 (C-12‴′, C-13‴′), 121.4 (C-2‴′, C-7‴′), 119.2 (C-5), 115.8 (C-4‴′, C-5‴′), 87.8 (C-1′), 82.4 (C-4′), 72.7 (C-2′), 71.0 (C-3′), 51.5 (N_{10}‴′-CH_2-), 48.8 (C-5′), 34.4 (-4″-CH_2-). ESI-HRMS calculated for $C_{28}H_{27}N_{10}O_5$: $[M+H]^+$ (m/z): 583.2167, found: 583.2134.

*6.30. N-((1-((5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl)-3,4,5-trimethoxybenzamide (**11o**).* Yield (244.0 mg, 45%), white powder, m.p. 230–232°C; $R_f = 0.38$ (CH_2Cl_2/MeOH 5 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.93 (t, $J = 5.4$ Hz, 1H, CONH), 8.29 (s, 1H, H-8), 8.16 (s, 1H, H-2), 7.87 (s, 1H, H-5″), 7.28 (s, 2H, 6-NH_2), 7.20 (s, 2H, H-2′‴, H-6′‴), 5.91 (d, $J = 5.4$ Hz, 1H, H-1′), 5.59 (d, $J = 5.4$ Hz, 1H, 3′-OH), 5.46 (d, $J = 4.8$ Hz, 1H, 2′-OH), 4.74 (m, 2H, 4″-CH_2-), 4.67 (m, 1H, H-2′), 4.46 (m, 2H, H-5′), 4.27 (m, 2H, H-3′, H-4′), 3.81 (s, 6H, 3′‴-OCH_3, 5′‴-OCH_3), 3.70 (s, 3H, 4′‴-OCH_3); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 165.5 (CONH), 156.1 (C-6), 152.7 (C-2), 152.5 (C-3′‴, C-5′‴), 149.3 (C-4), 145.0 (C-4″), 139.9 (C-8), 140.0 (C-4), 129.2 (C-1), 123.7 (C-5′), 119.2 (C-5), 104.8 (C-2′‴, C-6′‴), 87.7 (C-1′), 82.4 (C-4′), 72.6 (C-2′), 71.0 (C-3′), 60.1 (4′‴-OCH_3), 56.0 (3′‴-OCH_3, 5′‴-OCH_3), 51.2 (C-5′), 34.7 (4′-CH_2-). ESI-HRMS calculated for $C_{23}H_{28}N_9O_7$: $[M+H]^+$ (m/z): 542.2112, found: 542.2104.

6.31. N-((1-((5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl)-2-(4-methoxyphenyl)acetamide (11p). Yield (213.4 mg, 43%), white powder, m.p. 158–160°C; $R_f = 0.39$ (CH_2Cl_2/MeOH 5 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.38 (t, $J = 5.4$ Hz, 1H, CONH), 8.27 (s, 1H, H-8), 8.16 (s, 1H, H-2), 7.78 (s, 1H, H-5″), 7.29 (s, 2H, 6-NH_2), 7.13 (m, 2H, H-2′‴, H-6′‴), 6.83 (m, 2H, H-3′‴, H-5′‴), 5.91 (d, $J = 5.4$ Hz, 1H, H-1′), 5.59 (d, $J = 6.0$ Hz, 1H, 3′-OH), 5.46 (d, $J = 5.4$ Hz, 1H, 2′-OH), 4.74 (m, 2H, 4′-CH_2-), 4.67 (m, 1H, H-2′), 4.25 (m, 2H, H-5′), 4.23 (m, 2H, H-3′, H-4′), 3.71 (s, 3H, 4′‴-OCH_3), 3.32 (m, 2H, 1′‴-CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 170.3 (CONH), 157.9 (C-4′‴), 156.1 (C-6), 152.6 (C-2), 149.3 (C-4), 144.7 (C-4′), 139.9 (C-8), 129.9 (C-2′‴, C-6′‴), 128.1 (C-1′‴), 125.4 (C-5″), 119, 2 (C-5), 113.6 (C-3′‴, C-5′‴), 87.8 (C-1′), 82.4 (C-4′), 72.6 (C-2′), 71.0 (C-3′), 55.0 (4′‴-OCH_3), 51.4 (C-5′), 41.2 (1′‴-CH_2-), 34.1 (4′-CH_2-). ESI-HRMS calculated for $C_{22}H_{26}N_9O_5$: $[M+H]^+$ (m/z): 496.2058, found: 496.2049.

6.32. N-((1-((5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl)-2-(3-benzoylphenyl)propanamide (11q). Yield (262.9 mg, 45%), white powder, m.p. 140–142°C; $R_f = 0.37$ (CH_2Cl_2/MeOH 5 : 1 v/v); ^{1}H-NMR (600 MHz, DMSO-d_6, δ (ppm)): 8.46 (m, 1H, -CONH-), 8.27 (d, $J = 4.2$ HZ, 1H, H-8), 8.15 (s, 1H, H-2), 7.69 (m, 5H, H-5″, H-3‴, H-7‴, H-5‴, H-5′″), 7.56 (m, 4H, H-4‴, H-6‴, H-7′″, H-9′″), 7.45 (m, 1H, H-8′″), 7.28 (s, brd, 2H, 6-NH_2), 5.90 (d, $J = 6.0$ Hz, 1H, H-1′), 5.58 (d, $J = 6.0$ Hz, 1H, 3′-OH), 5.44 (d, $J = 4.8$ Hz, 1H, 2′-OH), 4.71 (m, 3H, 4″-CH_2-, H-2′), 4.26 (m, 3H, H-4′, H-3′, H-2′″), 4.16 (m, 1H, H-5′a), 3.71 (m, 1H, H-5′b), 1.32 (d, $J = 7.2$ Hz, 3H, H-3′″); ^{13}C-NMR (150 MHz, DMSO-d_6, δ (ppm)): 195.7 (C-1′‴′), 172.7 (C-1′″), 156.1 (C-6), 152.6 (C-2), 149.2 (C-4), 144.5 (C-4″), 142.5 (C-4′″), 139.9 (C-8), 137.0 (C-2′‴′), 136.8 (C-6′″), 132.6 (C-5′‴′), 131.5 (C-9′″), 129.9 (C-3′‴′, C-7′‴′), 128.5 (C-4′″, C-8′″), 128.4 (C-6′‴′), 128.0 (C-5′″), 123.4 (C-5″), 119.2 (C-5), 87.8 (C-1′), 82.4 (C-4′), 72.5 (C-2′), 71.0 (C-3′), 51.4 (C-5′), 44.6 (C-2′″), 34.2 (4″-CH_2-), 18.4 (C-3′″). ESI-HRMS calculated for $C_{29}H_{30}N_9O_5$: $[M + H]^+$ (m/z): 584.2371, found: 584.2360.

6.33. Biological Assays. The *in vitro* anti-inflammatory activity of all prepared products was determined using the nitrite assay in murine macrophages following published methods with minor modifications [56, 57].

The *in vitro* cytotoxic evaluation of the selected products against HepG2 and LU-1 cancer cell lines was carried out according to the described methods [58, 59].

The ACE2 and $3CL^{pro}$ inhibitory activities of the tested compounds were determined in accordance with the manufacturer's instructions for the ACE2 inhibitor screening kit (MAK378, Merck KGaA, Darmstadt, Germany) [60] and $3CL^{pro}$ kit (the untagged $3CL^{pro}$ (SAR-CoV-2) assay kit, Bioscience, San Diego CA, US) [61].

Data Availability

The data used to support the study can be made available upon request to the corresponding author.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Duc Anh Le, Ngoc Hung Truong, Khac Vu Tran, and Van Chinh Luu contributed equally to this work.

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