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ORIGINAL RESEARCH

Synthesis and antiviral activity evaluation of some new cyclohexylidenehydrazide derivatives of 1,3-thiazole core

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ABSTRACT

Six novel cyclohexylidenehydrazide derivatives carrying five membered heterocyclic ring, 1,3-thiazole were synthesized to investigate their antiviral (including anti-HIV) activity against diverse DNA and RNA viruses in CRFK, HeLa, HEL, MDCK, Vero and MT4 cell cultures. None of the compounds was found active against any of the DNA or RNA viruses at 100 μM.

Keywords: 1,3-Thiazole, cyclohexylidenehydrazide, antiviral activity

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INTRODUCTION

Viruses are the most common cause of global infectious disease. Viruses with high infection rates and rapid propagation can cause worldwide human and animal pandemics. Despite significant advances especially in antiviral therapy, there is continued interest in developing new agents for the treatment of viral diseases. The thiazole ring system is commonly found in many pharmaceutically important molecules. Numerous natural products containing this heterocycle have been isolated and exhibit significant biological activities (1). Thiazole plays vital roles in many drug structures. Ritonavir (anti-HIV drug) (2), Dasatinib and Tiazofurin (antineoplastic agents) (3), Fanetizole, Fentiazac and Meloxicam (anti-inflammatory agents) (4), Nizatidine (antiulcer agent) (5), Ravuconazole (antifungal agent) (6), Nitazoxanide (antiparasitic agent) (7) are some examples of thiazole bearing products (**Figure 1**) (8).

On the other hand, several hydrazide-ketone hydrazone derivatives have been reported to possess varios biological activities (9) such as, antiviral (10), antineoplastic (11), antituberculostatic (12, 13), analgesic (14), antibacterial (15), antifungal (16) activities.

In view of these observations, we report here the synthesis, structural determination and antiviral evaluation of new six N^2-substituted cyclohexylidene-2-(2-aminothiazol-4-yl) acetohydrazides.

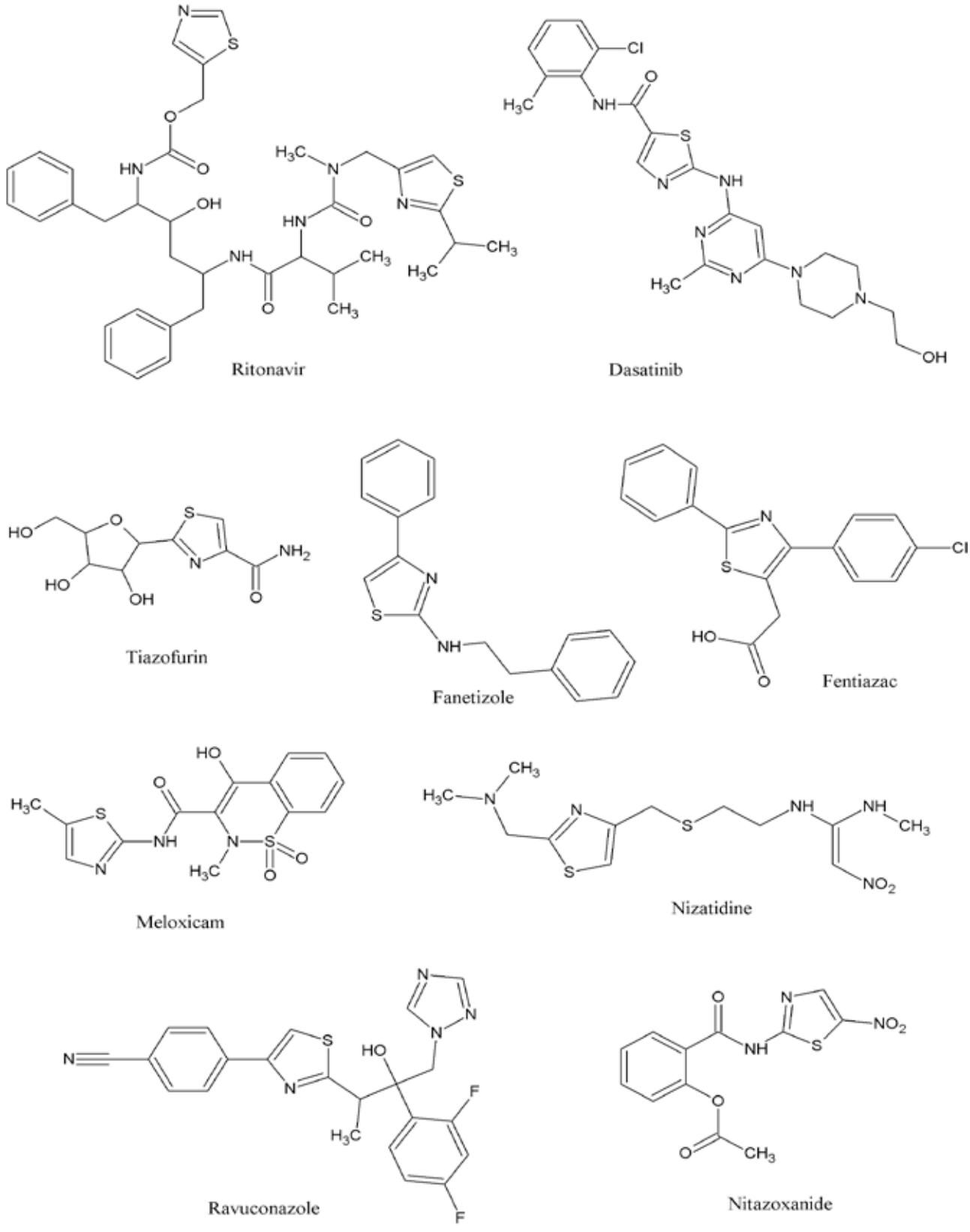


Figure 1. Examples of thiazole bearing drugs.

MATERIALS AND METHODS

Chemistry

Melting points were determined by using a Büchi B-540 melting point apparatus in open capillary tubes and are uncorrected. Elemental analyses were performed on a Thermo Finnigan Flash EA 1112 elemental analyzer. IR spectra were recorded on KBr discs, using a Shimadzu IR Affinity-1 FT-IR spectrophotometer. ^{1}H-NMR spectra were measured on a Varian UNITY INOVA (500 MHz) spectrometer using *DMSO*-d_6. The starting materials were commercially available.

Preparation of 2-(2-aminothiazol-4-yl)acetohydrazide (2)

To a solution of ethyl 2-(2-aminothiazol-4-yl)acetate (**1**) (0.005 mol) in ethanol (30 mL) were added hydrazine hydrate (0.025 mol, 98%). The reaction mixture was refluxed for 5h then cooled and allowed to stand overnight. The crystals were filtered, dried and purified by crystallization from ethanol.

General procedure for the synthesis of N^2-(substituted cyclohexylidene)-2-(2-aminothiazol-4-yl)acetohydrazides (3a-f)

A solution of substituted cyclohexanones (0.005 mol) and 2-(2-aminothiazol-4-yl)acetohydrazide (**2**) (0.005 mol) in absolute ethanol (30 ml) was refluxed for 6h and allowed to stand overnight. The crystals thus obtained were filtered, then recrystallized from ethanol.

*N^2-(3-methylcyclohexylidene)-2-(2-aminothiazol-4-yl) acetohydrazide (**3a**)*

Yield 80%; mp: 191-192°C; IR (KBr) ν_{max} (cm^{-1}): 3277 (N-H), 1685 (C=O). ^{1}H-NMR (DMSO-d_6) δ (ppm): 0.92; 0.95 (2d, 3H, *J*= 5.86; 6.35 Hz, CH_3), 1.13-1.17 (m, 1H, cyclohexylidene C_3-H), 1.38-1.42 (m, 1H, cyclohexylidene $C_{5\text{-axial}}$H), 1.53-1.61 (m, 2H, cyclohexylidene $C_{4\text{-axial}}$H ve $C_{5\text{-equatorial}}$H), 1.69-1.71 (m, 1H, cyclohexylidene $C_{2\text{-axial}}$H), 1.80-1.84 (m, 1H, cyclohexylidene $C_{4\text{-equatorial}}$H), 2.04-2.10 (m, 1H, cyclohexylidene $C_{6\text{-axial}}$H), 2.25-2.27 (m, 1H, cyclohexylidene $C_{6\text{-equatorial}}$H), 2.76; 2.87 (2d, 1H, *J*= 10.73 Hz, cyclohexylidene $C_{2\text{-equatorial}}$H), 3.36; 3.68 (2s, 2H, CH_2CO), 6.18; 6.25 (2s, 1H, thiazole C_5-H), 6.75; 6.86 (2s, 2H, NH_2), 10.17; 10.28 (2s, 1H, CONH). Anal. Calcd. for $C_{12}H_{18}N_4OS$: C, 54.11; H, 6.81; N, 21.03; Found: C, 54.02; H, 6.56; N, 20.97.

*N^2-(4-methylcyclohexylidene)-2-(2-aminothiazol-4-yl) acetohydrazide (**3b**)*

Yield 73%; mp: 188-189°C; IR (KBr) ν_{max} (cm^{-1}): 3367 (N-H), 1653 (C=O). ^{1}H-NMR (DMSO-d_6) δ (ppm): 0.91 (d, 3H, *J*= 6.34 Hz, CH_3), 1.00-1.15 (m, 2H, cyclohexylidene C_4-H ve $C_{3\text{-axial}}$H/$C_{5\text{-axial}}$H), 1.62-1.69 (m, 1H, cyclohexylidene $C_{3\text{-axial}}$H/$C_{5\text{-axial}}$H), 1.74-1.91 (m, 3H, cyclohexylidene $C_{3\text{-equatorial}}$H, $C_{5\text{-equatorial}}$H ve $C_{2\text{-axial}}$H/$C_{6\text{-axial}}$H), 2.13-2.21 (m, 1H, cyclohexylidene $C_{2\text{-axial}}$H/$C_{6\text{-axial}}$H), 2.25-2.32 (m, 1H, cyclohexylidene $C_{2\text{-equatorial}}$H/$C_{6\text{-equatorial}}$H), 2.81; 2.92 (2d, 1H, *J*= 14.64 Hz, cyclohexylidene $C_{2\text{-equatorial}}$H/$C_{6\text{-equatorial}}$H), 3.35; 3.68 (2s, 2H, CH_2CO), 6.19; 6.25 (2s, 1H, thiazole C_5-H), 6.78; 6.90 (2s, 2H, NH_2), 10.21; 10.32 (2s, 1H, CONH). Anal. Calcd. for $C_{12}H_{18}N_4OS$: C, 54.11; H, 6.81; N, 21.03; Found: C, 53.19; H, 7.03; N, 21.25.

*N^2-(4-ethylcyclohexylidene)-2-(2-aminothiazol-4-yl) acetohydrazide (**3c**)*

Yield 74%; mp: 181-182°C; IR (KBr) ν_{max} (cm^{-1}): 3373 (N-H), 1656 (C=O). ^{1}H-NMR (DMSO-d_6) δ (ppm): 0.87 (t, 3H, *J*= 7.32 Hz, CH_3), 0.93-1.12 (m, 2H, cyclohexylidene C_4-H ve $C_{3\text{-axial}}$H/$C_{5\text{-axial}}$H), 1.20-1.27 (m, 2H, CH_2), 1.40-1.44 (m, 1H, cyclohexylidene $C_{3\text{-axial}}$H/$C_{5\text{-axial}}$H), 1.77-1.90 (m, 3H, cyclohexylidene $C_{3\text{-equatorial}}$H, $C_{5\text{-equatorial}}$H ve $C_{2\text{-axial}}$H/$C_{6\text{-axial}}$H), 2.12-2.19 (m, 1H, cyclohexylidene $C_{2\text{-axial}}$H/$C_{6\text{-axial}}$H), 2.27-2.33 (m, 1H, cyclohexylidene $C_{2\text{-equatorial}}$H/$C_{6\text{-equatorial}}$H), 2.82; 2.93 (2d, 1H, *J*= 15.61; 14.15 Hz, cyclohexylidene $C_{2\text{-equatorial}}$H/$C_{6\text{-equatorial}}$H), 3.43; 3.69 (2s, 2H, CH_2CO), 6.19; 6.25 (2s, 1H, thiazole C_5-H), 6.78; 6.90 (2s, 2H, NH_2), 10.20; 10.33 (2s, 1H, CONH). Anal. Calcd. for $C_{13}H_{20}N_4OS$: C, 55.69; H, 7.19; N, 19.98; Found: C, 55.09; H, 7.75; N, 19.97.

*N^2-(4-propylcyclohexylidene)-2-(2-aminothiazol-4-yl) acetohydrazide (**3d**)*

Yield 39%; mp: 179-180°C; IR (KBr) ν_{max} (cm^{-1}): 3369 (N-H), 1658 (C=O). ^{1}H-NMR (DMSO-d_6) δ (ppm): 0.88 (t, 3H, *J*= 7.32 Hz, CH_3), 0.96-1.12 (m, 2H, cyclohexylidene C_4-H ve $C_{3\text{-axial}}$H/$C_{5\text{-axial}}$H), 1.17-1.23 (m, 2H, cyclohexylidene 4-C$\underline{H}_2$$CH_2CH_3$), 1.26-1.33 (m, 2H, cyclohexylidene 4-$CH_2C\underline{H}_2CH_3$), 1.49-1.55 (m, 1H, cyclohexylidene $C_{3\text{-axial}}$H/$C_{5\text{-axial}}$H), 1.78-1.90 (m, 3H, cyclohexylidene $C_{3\text{-equatorial}}$H, $C_{5\text{-equatorial}}$H ve $C_{2\text{-axial}}$H/$C_{6\text{-axial}}$H), 2.12-2.20 (m, 1H, cyclohexylidene $C_{2\text{-axial}}$H/$C_{6\text{-axial}}$H), 2.26-2.33 (m, 1H, cyclohexylidene $C_{2\text{-equatorial}}$H/$C_{6\text{-equatorial}}$H), 2.82; 2.93 (2d, 1H, *J*= 15.13; 15.62 Hz, cyclohexylidene $C_{2\text{-equatorial}}$H/$C_{6\text{-equatorial}}$H), 3.35; 3.68 (2s, 2H, CH_2CO), 6.18; 6.25 (2s, 1H, thiazole C_5-H), 6.78; 6.90 (2s, 2H, NH_2), 10.20; 10.32 (2s, 1H, CONH). Anal. Calcd. for $C_{14}H_{22}N_4OS$: C, 57.11; H, 7.53; N, 19.03; Found: C, 56.20; H, 7.61; N, 19.58.

*N^2-(4-tert-butylcyclohexylidene)-2-(2-aminothiazol-4-yl) acetohydrazide (**3e**)*

Yield 82%; mp: 157-158°C; IR (KBr) ν_{max} (cm^{-1}): 3402 (N-H), 1660 (C=O). ^{1}H-NMR (DMSO-d_6) δ (ppm): 0.85 (s, 9H, cyclohexylidene 4-$C(CH_3)_3$), 1.04-1.15 (m, 2H, cyclohexylidene C_4-H ve $C_{3\text{-axial}}$H/$C_{5\text{-axial}}$H), 1.26-1.29 (m, 1H, cyclohexylidene $C_{3\text{-axial}}$H/$C_{5\text{-axial}}$H), 1.79-1.90 (m, 3H, cyclohexylidene $C_{3\text{-equatorial}}$H, $C_{5\text{-equatorial}}$H ve $C_{2\text{-axial}}$H/$C_{6\text{-axial}}$H), 2.12-2.16 (m, 1H, cyclohexylidene $C_{2\text{-axial}}$H/$C_{6\text{-axial}}$H), 2.34-

2.37 (m, 1H, cyclohexylidene $C_{2\text{-equatorial}}H/C_{6\text{-equatorial}}H$), 2.89; 3.02 (2d, 1H, *J*= 14.64 Hz, cyclohexylidene $C_{2\text{-equatorial}}H/C_{6\text{-equatorial}}H$), 3.35; 3.68 (2s, 2H, CH_2CO), 6.18; 6.25 (2s, 1H, thiazole C_5-H), 6.75; 6.88 (2s, 2H, NH_2), 10.16; 10.31 (2s, 1H, CONH). Anal. Calcd. for $C_{15}H_{24}N_4OS$: C, 58.41; H, 7.84; N, 18.16; Found: C, 58.26; H, 7.68; N, 18.12.

*N^2-(4-phenylcyclohexylidene)-2-(2-aminothiazol-4-yl) acetohydrazide (**3f**)*

Yield 91%; mp: 209-210°C; IR (KBr) ν_{max} (cm^{-1}): 3365 (N-H), 1658 (C=O). ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.51-1.59 (m, 1H, cyclohexylidene $C_{3\text{-axial}}H/C_{5\text{-axial}}H$), 1.60-1.70 (m, 1H, cyclohexylidene $C_{3\text{-axial}}H/C_{5\text{-axial}}H$), 1.90-2.05 (m, 2H, cyclohexylidene $C_{3\text{-equatorial}}H$ ve $C_{5\text{-equatorial}}H$), 2.32-2.49 (m, 3H, cyclohexylidene $C_{2\text{-axial}}H$, $C_{6\text{-axial}}H$ ve $C_{2\text{-equatorial}}H/C_{6\text{-equatorial}}H$), 2.82-2.87 (m, 1H, cyclohexylidene C_4-H), 3.01; 3.13 (2d, 1H, *J*= 15.62; 15.61 Hz, cyclohexylidene $C_{2\text{-equatorial}}H/C_{6\text{-equatorial}}H$), 3.38; 3.73 (2s, 2H, CH_2CO), 6.22; 6.27 (2s, 1H, thiazole C_5-H), 6.80; 6.91 (2s, 2H, NH_2), 7.17-7.30 (m, 5H, phenyl), 10.30; 10.41 (2s, 1H, CONH). Anal. Calcd. for $C_{17}H_{20}N_4OS$: C, 62.17; H, 6.14; N, 17.06; Found: C, 61.78; H, 6.26; N, 17.26.

Biological activity

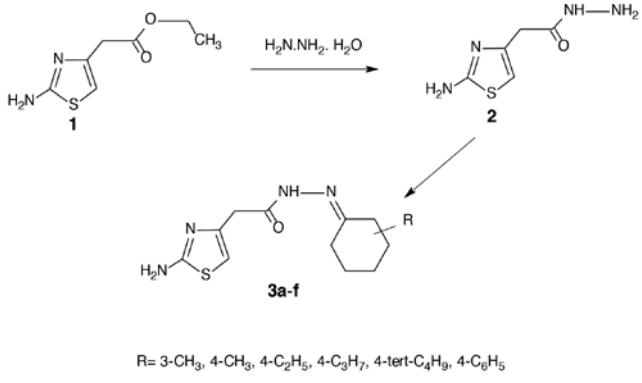
Antiviral evaluations in cell culture

The compounds (**3a**-**f**) were evaluated for activity against diverse RNA- and DNA-viruses, using the following cell-based assays (17): (a) Crandell-Rees Feline Kidney (CRFK) cells infected with Feline corona virus or Feline herpes virus; (b) Human embryonic lung (HEL) fibroblast cells infected with Herpes simplex virus-1 or -2, Vaccinia virus, Vesicular stomatitis virus, an Acyclovir-resistant herpes simplex virus-1 strain, or Adenovirus-2; (c) Human cervixcarcinoma HeLa cells infected with Vesicular stomatitis virus, Coxsackie B4 virus or Respiratory syncytial virus; (d) African green monkey kidney Vero cells infected with Para-influenza-3 virus, Reovirus-1, Sindbis virus, Coxsackie B4 virus, Punta toro virus or Yellow fever virus; (e) Madin-Darby canine kidney (MDCK) cells infected with Influenza A/H1N1 subtype (A/Ned/378/05), Influenza A/H3N2 subtype (A/HK/7/87) or Influenza B (B/Ned/537/05); and (f) Human T-lymphoblast MT4- cells infected with HIV-1 or HIV-2.

To perform the antiviral assays, the virus was added to subconfluent cell cultures in 96-well plates, and at the same time, the test compounds were added at serial dilutions. Appropriate reference compounds were included, i.e. the virus entry inhibitor dextran sulfate 5000, the broad antiviral agent ribavirin, the antiherpetic drug ganciclovir, and the HIV inhibitor azidothymidine. After 3-6 days incubation at 37 °C (or 35 °C in the case of influenza virus), the cultures were examined by microscopy to score the compounds' inhibitory effect on virus-induced cytopathic effect (CPE) or their cytotoxicity. For some viruses [Influenza A/H1N1 (A/Ned/378/05), Influenza A/H3N2 (A/HK/7/87) and Influenza B (B/Ned/537/05)] antiviral and cytotoxic activities were confirmed by the colorimetric MTS cell viability assay.

RESULTS AND DISCUSSION

2-(2-Aminothiazol-4-yl)acetic acid hydrazide (**2**) was prepared from ethyl 2-(2-aminothiazol-4-yl)acetate (**1**) according to a previously published procedure (18). Condensation of **2** with substituted cyclohexanones afforded the corresponding N^2-substituted cyclohexylidene-2-(2-aminothiazol-4-yl) acetohydrazides (**3a**-**f**) (Scheme 1). The structures of the obtained compounds were elucidated by spectral data. The IR spectra of **3a**-**f** showed two separate bands resulting from the N-H and C=O streching bands of the amide function at about regions 3402-3277 and 1685-1653 cm^{-1}, respectively (19, 20). In the spectra of ^{1}H-NMR of **3a**-**f** the CH_2 and CONH of the acetylamino moiety were observed as a double singlets presumably due to the partial double bond character of the C-N bond and the bulk of the attached cyclohexyl structure which can disrupt free rotation about the cited bond (δ 3.73-3.35 and δ 10.41-10.16 ppm, respectively) (21). The protons of the 1,3-thiazole and substituted cyclohexylidene nucleus resonated at the expected regions (22-25).



Scheme 1. The synthetic pathway of the title compounds **(3a-f).**

The synthesized compounds were evaluated against a broad and diverse panel of RNA- and DNA-viruses using cytopathic effect (CPE) reduction assays in appropriate cell culture models (17). As can be seen in Tables 1-6, none of the synthesized compounds was found active (i.e. minimal antivirally effective concentration ≥5-fold lower than minimal cytotoxic concentration) against any of the DNA or RNA viruses, including HIV virus at 100 μM.

Table 1. Anti-feline corona virus (FIPV) and anti-feline herpes virus activity and cytotoxicity of the compounds **3a**-**3f** in CRFK cell cultures.

Compound	CC_{50}[a] (μM)	EC_{50}[b] (μM)	
		Feline Corona Virus (FIPV)	Feline Herpes Virus
3a	>100	>100	>100
3b	>100	>100	>100
3c	>100	>100	>100
3d	>100	>100	>100
3e	>100	>100	>100
3f	>100	>100	>100
HHA (μg/ml)	>100	11	2.9
UDA (μg/ml)	>100	3.3	1.6
Ganciclovir (μM)	>100	>100	2.2

[a]50% Cytototoxic concentration, as determined by measuring the cell viability with the colorimetric formazan-based MTS assay.

[b]50% Effective concentration, or concentration producing 50% inhibition of virus-induced cytopathic effect, as determined by measuring the cell viability with the colorimetric formazan-based MTS assay.

Table 2. Antiviral activity and cytotoxicity of the compounds **3a**-**3f** in HEL cell cultures.

Compound	MCC[a] (μM)	EC_{50}[b] (μM)					
		Herpes simplex virus-1 (KOS)	Herpes simplex virus-2 (G)	Herpes simplex virus-1 TK^- KOS ACV^r	Vaccinia virus	Adenovirus-2	Vesicular stomatitis virus
3a	>100	>100	>100	>100	>100	>100	>100
3b	>100	>100	>100	>100	>100	>100	>100
3c	>100	>100	>100	>100	>100	>100	>100
3d	>100	>100	>100	>100	>100	>100	>100
3e	>100	>100	>100	>100	>100	>100	>100
3f	>100	>100	>100	>100	>100	>100	>100
Brivudin	>250	0.04	250	>250	6.8	-	>250
Cidofovir	>250	2.0	0.80	1.2	6.8	19	>250
Acyclovir	>250	0.4	0.2	125	>250	-	>250
Ganciclovir	>100	0.06	0.03	4.0	>100	-	>100
Zalcitabine	>250	-	-	-	-	15	-
Alovudine	>250	-	-	-	-	22	-

[a]Required to cause a microscopically detectable alteration of normal cell morphology.

[b]Required to reduce virus-induced cytopathogenicity by 50 %.

Table 3. Antiviral activity and cytotoxicity of the compounds **3a**-**3f** in HeLa cell cultures.

	Cytotoxicity (μM)	Antiviral EC_{50}[b] (μM)		
Compound	**MCC[a]**	**Vesicular stomatitis virus**	**Coxsackie virus B4**	**Respiratory syncytial virus**
3a	>100	>100	>100	>100
3b	>100	>100	>100	>100
3c	>100	>100	>100	>100
3d	>100	>100	>100	>100
3e	>100	>100	>100	>100
3f	>100	>100	>100	>100
DS-10000 (μg/ml)	>100	0.8	34	0.4
Ribavirin (μM)	>250	26	112	5.8

[a]Required to cause a microscopically detectable alteration of normal cell morphology.

[b]Required to reduce virus-induced cytopathogenicity by 50 %.

Table 4. Antiviral activity and cytotoxicity of the compounds **3a**-**3f** in Vero cell cultures.

Compound	**MCC[a] (μM)**	Antiviral EC_{50}[b] (μM)					
		Para-influenza-3 virus	**Reovirus-1**	**Sindbis virus**	**Coxsackie virus B4**	**Punta Toro virus**	**Yellow Fever virus**
3a	>100	>100	>100	>100	>100	>100	>100
3b	>100	>100	>100	>100	>100	>100	>100
3c	>100	>100	>100	>100	>100	>100	>100
3d	>100	>100	>100	>100	>100	>100	>100
3e	>100	>100	>100	>100	>100	>100	>100
3f	>100	>100	>100	>100	>100	>100	>100
DS-10000 (μM)	>100	>100	>100	4.0	58	100	0.60
Ribavirin (μM)	>250	146	112	>250	>250	112	250
Mycophenolic acid (μM)	>100	0.8	2.0	4.0	>250	10	1.8

[a]Required to cause a microscopically detectable alteration of normal cell morphology.

[b]Required to reduce virus-induced cytopathogenicity by 50 %.

Table 5. Anti-influenza virus activity and cytotoxicity of compounds **3a**-**3f** in MDCK cell cultures.

Compound	Cytotoxicity (μM)		Influenza A/H1N1 (A/Ned/378/05)[c]		Influenza A/H3N2 (A/HK/7/87)[c]		Influenza B (B/Ned/537/05)[c]	
	CC_{50}[a]	MCC[b]	CPE	MTS	CPE	MTS	CPE	MTS
3a	>100	>100	>100	>100	>100	>100	>100	>100
3b	>100	>100	>100	>100	>100	>100	>100	>100
3c	>100	>100	>100	>100	>100	>100	>100	>100
3d	>100	>100	>100	>100	>100	>100	>100	>100
3e	>100	>100	>100	>100	>100	>100	>100	>100
3f	>100	>100	>100	>100	>100	>100	>100	>100
Zanamivir	>100	>100	0.8	0.4	0.5	1.5	0.4	0.8
Ribavirin	>100	>100	8.9	7.0	8.9	7.6	2.6	6.7
Amantadine	>200	>200	40	13.7	0.8	0.8	>200	>200
Rimantadine	>200	>200	1.6	0.8	0.8	0.7	>200	>200

[a]50%Cytotoxic concentration, as determined by measuring the cell viability with the colorimetric formazan-based MTS assay.

[b]Minimum compound concentration that causes a microscopically detectable alteration of normal cell morphology.

[c]EC_{50}: 50% effective concentration or concentration producing 50% inhibition of virus-induced cytopathic effect, as determined by visual scoring of the cytopathic effect (CPE) or by measuring the cell viability with the colorimetric formazan-based MTS assay.

Table 6. Anti-HIV activity and cytotoxicity of the compounds **3a**-**3f** in MT4 cells[a].

Compound	Cytotoxicity (μM)	Antiviral EC_{50} (μM)	
	CC_{50}	HIV-1 (strain IIIB)	HIV-1 (strain ROD)
3a	>125	>125	>125
3b	>125	>125	>125
3c	>125	>125	>125
3d	>125	>125	>125
3e	>125	>125	>125
3f	>125	>125	>125
Nevirapine (μg/ml)	>4	0.075	>4
Lamivudine (μg/ml)	>20	0.58	2.3
Azidothymidine (μg/ml)	>2	0.0020	0,0022
Didanosine (μg/ml)	>50	18	19

[a]Antiviral activity and cytotoxicity were determined by the colorimetric MTS cell viability assay. The antiviral EC_{50} represents the compound concentration producing 50% inhibition of virus-induced cytopathicity. The CC_{50} represents the compound concentration causing 50% reduction of cell viability.

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1,3-Tiyazol Halkası Taşıyan Bazı Yeni Siklohekzilidenhidrazit türevlerinin sentezi ve antiviral etkileri

ÖZ

5 Üyeli heterosiklik halka olarak 1,3-tiyazol halkası taşıyan sikloheksilidenhidrazit türevi 6 yeni bileşik sentezlenmiş ve CRFK, HeLa, HEL, MDCK, Vero ve MT4 hücre kültürlerinde çeşitli DNA ve RNA virüslerine karşı antiviral aktiviteleri (HIV dahil) incelenmiştir. Bileşiklerin hiçbirinde 100 μM'da DNA ve RNA virüslerine karşı aktivite saptanmamıştır.

Anahtar kelimeler: 1,3-Tiyazol, sikloheksilidenhidrazit, antiviral aktivite

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