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Synthesis, Characterization and Antiviral Activity of Chrysin Derivatives

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In this work, the isolation of chrysin (**1**), which is a significant constituent from hexanes concentrate of *Derris scandens* is reported. A progression of new 1,2,3-triazole subsidiaries of chrysin were planned, combined and assessed for their antiviral movement against newcastle disease virus (NDV) and blue tongue virus (BTV) cell lines. These synthetic derivatives have indicated great antiviral action. All the synthesized compounds (**3a** to **3g**) were distinguished by using nuclear magnetic resonance (NMR) and mass spectroscopic techniques. Among derivatives, **3a**, **3e**, **3f** and **3g** displayed conspicuous action against NDV, then again compounds **3a**, **3b**, **3c**, **3e**, **3f** and **3g** showed a remarkable action against BTV than chrysin.

Keywords: Chrysin derivatives, *Derris scandens*, Blue tongue virus.

INTRODUCTION

Flavonoids have been demonstrated to decrease acute HIV-1 infection in H9 and C8166 cultures, as well as evidence of flavonoids inhibiting HIV-1 protease, integrase and reverse transcriptase. The regular isoflavone chrysin confined from *Derris scandens* Benth and is one of the main bioactive constituents of various natural products, vegetables and even mushrooms [1]. Several *in vitro* and *in vivo* research have demonstrated that chrysin has therapeutic properties against a variety of disorders. Heterocyclic nitrogen compounds are omnipresent in the environment, these are present in various proteins, nucleotides, peptides, nutrients and coenzymes, are seen through characteristic items, for example, alkaloids [2-4]. Because of the wide range of qualities displayed by heterocyclic compounds contain nitrogen atom, individuals from this chemical classification, such as triazoles, are often used in the pharmaceutical industry for these structural blocks [5,6].

1,2,3-Triazole and 1,2,4-triazole rings are the most common heterocyclic rings found in different therapeutic specialities [7-9]. Triazole compounds are intriguing interfacing units because they are resistant to metabolic decomposition and can store hydrogen, which is beneficial in the official of biomolecular targets and so they have increased bioavailability [10-12]. There are numerous compounds containing the triazole analogue that have a variety of organic properties, such as antiviral activity, disease resistance, antiproliferative, antibacterial activities, *etc*. and those were combined before the methodology of click chemistry was developed [13-16]. In this situation, a mixture of 1,2,3-triazoles and chrysin should have high action and selectivity, drug-similarity and great pharmacokinetic properties. The promising biological profiles of flavonoids, notably chrysin, as well as our present research interests in finding and developing antiviral agents from natural resources [17], prompted us to use copper-catalyzed click chemistry to incorporate the novel triazole derivatives of chrysin and test their natural characteristics for antiviral activity.

EXPERIMENTAL

Whole plant materials (leaves, stem and bark) of *D. scandens* were collected from forest located in Andhra Pradesh state, India. The plant was authenticated by Department of Botany, GITAM University, India. The authenticated sample was submitted in GITAM University herbarium, India.

The NMR spectra for ^{1}H and ^{13}C were recorded separately on a Bruker 300 MHz spectrometer, with TMS as a standard. Chemical shifts were expressed in parts per million (ppm), while coupling constants (*J*) were expressed in hertz (Hz). An

Agilent Technologies 6510 Q-TOF Mass Spectrometer was used to collect mass spectra. Chromatography was carried out on a silica gel (100-200 lattice, Qingdao Marine Chemical, Inc., Qingdao, China), with ethyl acetate and hexane as eluents. Under the nitrogen climate, reactions that required the use of anhydrous, latent environment technologies were accomplished. Without any further refinement, industrially available reagents, solvents and starting ingredients were used. Scientific TLC was done with the dissolvable framework ethyl acetate/hexane on recoated Merck plates (60 F_{254}, 0.2 mm) and the mixtures were seen under UV light and showered with 10% H_2SO_4 followed by heat.

Source of virus and eggs: NDV and BTV cell lines and emb-ryonated eggs were collected from Virology and Poultry Departments of Sri Venkateswara University, Tirupati, India. The collected eggs were hatched at 37 ºC.

Cell line collection and preservation: The National Centre for Cell Sciences in Pune provided BHK-21cell lines. The cell lines were kept at 37 ºC in Dulbecco's Modified Eagle Medium (DMEM) containing 5% serum, 2% FBS, 100 µg/mL penicillin and 100 µg/mL streptomycin in water-soaked air containing 5% CO_2. Tripsinization was used to pass the crossing cells once a week [18].

***in ovo* antiviral activity:** The mobility of derivatives was assessed using 9 day-old hatching eggs. Cleaning the eggs with 70% liquor and placing them in a sterile plate was done. The eggs were cleaned and used to administer the derivative/virus cocktail *via* the allantoic method. In 0.1 mL of NDV/BTV in 0.1 mL of 1 mg/mL derivative in DMSO, the derivative/viral mixture was suspended (DMSO). Controls included virus dissolved in saline (without derivative).

Nine days of age NDV-injected chick embryos were inoculated using preserved viruses and their controls through CAM and the egg yolk sac in the investigation. Two viral samples were produced in triplicate against each derivative and compared to a control sample. The eggs were sealed with molten wax and then incubated at 37 ºC. To identify NDV, allantoic fluid from treated eggs were taken [19].

A set number (5×10^6) of exponentially proliferating NDV/BTV infected cells were planted into 96 well microtiter plates and allowed to proliferate. The virus mixture was made by suspending 0.1 mL of NDV/BTV in 0.1 mL of 1 mg/mL derivative in DMSO, 100 mL of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2*H*-tetrazolium bromide (MTT) for 3 h, followed by 10 mL dissolution solution and mixing vigorously with a pipette/glass rod. The MTT medium was carefully removed from the wells and the formazan dye was eluted using DMSO. At a wavelength of 570 nm, a multi-mode ELISA reader was used to detect absorbance [20].

***in ovo* Hemagglutination (HA) test:** The airspace in the egg shells was reduced after deceased embryos of eggs were placed in a biosafety cabinet. Collected blood samples were allowed for centrifugation at 1000 rpm with a period of 10 min, then saline was added, the supernatant was removed and an equal amount of sterile saline was added, centrifuged at 1000 rpm for another 10 min. This technique was performed three times and the packed RBCs were diluted to 1% for use in the Hemagglutination test. 0.025 mL of 1% RBC solution was added to each well. The results were evaluated after 30 min of incubation at room temperature [21,22].

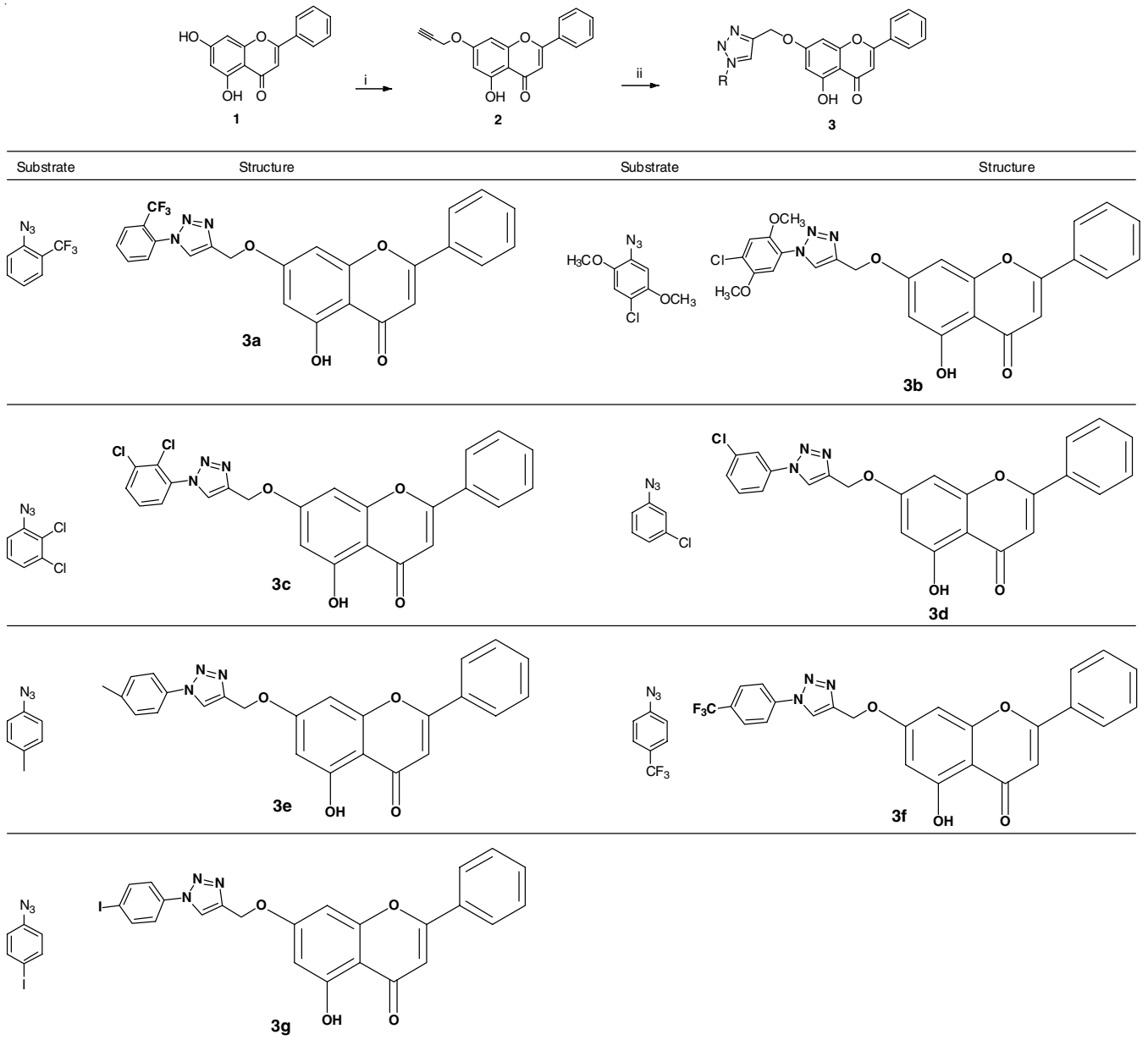
General procedure

Isolation of chrysin (1): Shade dried plant materials (5 kg) were grinded and extracted with Soxhlet, mechanical assembly in presence of *n*-hexane for 72 h. 1 bar vacuum applied during drying to attain *n*-hexane extract until a syrupy crude (50.0 g) formed. Collected crude was processed using Silica gel column chromatography (100-200 mesh and 150 × 7.5 cm dimensions) using mixture of petroleum ether and chloroform (in range of 100:0 to 5:95) to attain 20 cumulative fractions around 100-250 mL of each portion. TLC evaluation was performed for collected fractions using various mobile phase compositions of petroleum ether and ethyl acetate in ratio of 95:5 to 70:30 to select four major fractions. F1 fraction further treated using hexane:ethyl acetate mixture 95:5 using column chromatography to obtain chrysin derivative (**1**) [23].

Synthesis of propargylation of chrysin (2): Potassium carbonate was progressively added at room temperature under nitrogen environment to a 20 mL DMF solution containing 1.0 mmol chysin. At 0-5 ºC, propargyl bromide (1.3 mmol) was gently added for 5 min. After the addition, the reaction mass was allowed to heat up to 65 ºC and kept there until the SM is entirely converted, which is monitored by TLC. The reaction mass is concentrated at decreased pressure and purified using hexane: ethyl acetate column chromatography (80:20) [23]. Colour: light yellow colour solid. m.p.: 163-164 ºC. Yield: 87%. IR (KBr, ν_{max}, cm^{-1}): 3423, 3277, 3095, 1638, 1607, 1202, 816. ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.59 (1H, s), 7.69 (2H, m), 7.39 (3H, m), 6.60 (1H, s), 6.44 (d, *J* = 1.9 Hz, 1H), 6.29 (d, *J* = 1.9 Hz, 1H), 4.61 (d, *J* = 2.2 Hz, 2H), 2.49 (t, *J* = 2.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.92, 163.62, 162.87, 161.82, 157.13, 131.32, 130.74, 128.79, 125.79, 105.31, 98.33, 92.96, 76.82, 62.23. Calculated for HRESI-MS $C_{25}H_{17}N_3O_4F_3$: 293.0813 $[M+H]^+$. Observed: 293.0835 $[M+H]^+$.

Synthesis of chrysin triazol derivatives: Derivative-2 was added into a mixture of THF, triethylamine and copper(I) iodide. The batch was then heated to 60 ºC to complete the reaction conversion. The batch was then filtered and extracted with ethyl acetate [24,25]. The filtrate on evaporation gave solid, these solids on chromatography using ethyl acetate and hexane gave pure triazole derivatives of chrysin (**Scheme-I**).

5-Hydroxy-2-phenyl-7-((1-(2-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazol-5-yl)methoxy)-4*H*-chromen-4-one (3a): Colour: light yellow colour solid. m.p.: 165-167 ºC. IR (KBr, ν_{max}, cm^{-1}): 3455, 3072, 1663, 1615, 1159, 835. ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.74 (1H, s), 7.96 (1H, s), 7.91-7.78 (m, 3H), 7.76 (1H, t, *J* = 7.4, 15.1), 7.71 (1H, t, *J* = 7.4, 15.1), 7.60 (d, *J* = 8.7 Hz, 1H), 7.59-7.53 (m, 3H), 6.69 (s,1H), 6.67 (d, *J* = 2.1 Hz, 1H), 6.48 (d, *J* = 2.1 Hz, 1H), 5.40 (brs, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.48, 164.14, 163.95, 162.19, 143.08, 157.77, 143.08, 133.10, 131.88, 131.19, 130.62, 129.08, 128.99, 127.37, 127.28, 126.31, 125.65, 105.92, 106.14, 99.07, 93.32, 62.23. Calculated for HRESI-MS $C_{25}H_{17}N_3O_4F_3$: 480.1171 $[M+H]^+$. Observed: 480.1166 $[M+H]^+$.



Reagent and conditions: (i) acetone, K_2CO_3, propargyl bromide, 3-5 h, 65 °C (ii) CuI, R = aromatic azides, THF, triethyl amine, 6 h, 60 °C

Scheme-I

7-((1-(4-Chloro-2,5-dimethoxyphenyl)-1*H*-1,2,3-triazol-5-yl)methoxy)-5-hydroxy-2-phenyl-4*H*-chromen-4-one (3b): Colour: light yellow colour solid. m.p.: 171-172 ºC. Yield: 83%. IR (KBr, ν_{max}, cm^{-1}): 3461, 3064, 2925, 1651, 1622, 1351, 1160, 818. ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.73 (1H, s), 8.31 (1H, s), 7.89 (2H, dd, *J* = 1.6, 8.2 Hz), 7.55-7.53 (4H, m), 7.15 (1H, s), 6.68 (1H, d, *J* = 2.2 Hz), 6.69 (1H, s), 6.49 (1H, d, *J* = 2.2 Hz,), 5.38 (brs, 2H), 3.93 (s, 3H), 3.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.48, 164.13, 164.06, 162.17, 157.77, 149.54, 144.37, 142.63, 131.89, 131.21, 129.08, 126.32, 125.21, 124.65, 123.42, 114.91, 108.95, 106.07, 105.92, 99.06, 93.40, 62.29, 56.88, 56.77. Calculated for HRESI-MS $C_{26}H_{21}N_3O_6Cl$: 506.1189 $[M+H]^+$. Observed: 506.1179 $[M+H]^+$.

7-((1-(2,3-Dichlorophenyl)-1*H*-1,2,3-triazol-5-yl)-methoxy)-5-hydroxy-2-phenyl-4*H*-chromen-4-one (3c): Colour: yellow colour solid. m.p.: 160-161 ºC. Yield: 82%. IR (KBr, ν_{max}, cm^{-1}): 3474, 3085, 3009, 1657, 1616, 1349, 1158, 820. ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.74 (1H, s), 8.09 (1H, s), 7.90 (2H, dd, *J* = 1.8, 8.2 Hz), 7.67 (1H, dd, *J* = 1.3, 8.0), 7.57-7.53 (4H, m), 7.41 (t, *J* = 8.0, 1H), 6.69 (s, 1H), 6.68 (d, *J* = 2.2 Hz, 1H), 6.49 (d, *J* = 2.2 Hz,1H), 5.40 (brs, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.49, 165.10, 164.18, 163.94, 162.24, 157.78, 143.04, 136.23, 134.75, 131.91, 131.20, 130.16, 129.10, 127.94, 126.33, 126.15, 125.05, 105.95, 106.92, 99.01, 93.34, 62.22. Calculated for HRESI-MS $C_{24}H_{16}N_3O_4Cl_2$: 480.0519 $[M+H]^+$. Observed: 480.0528 $[M+H]^+$.

7-((1-(3-Chlorophenyl)-1*H*-1,2,3-triazol-5-yl)methoxy)-5-hydroxy-2-phenyl-4*H*-chromen-4-one (3d): Colour: pale yellow colour solid. m.p.: 158-159 ºC. Yield: 80%. IR (KBr, ν_{max}, cm^{-1}): 3489, 3081, 2965, 1661, 1607, 1501, 1365, 1161,

758. ^{1}H NMR (400 MHz, $CDCl_3$): 12.73 (1H, s), 8.01 (1H, s) 7.89-7.86 (1H, m), 7.65 (1H, dd, *J* = 2.2, 9.6 Hz), 7.60 (1H, dd, *J* = 2.2, 9.6 Hz), 7.54-7.52 (2H, m), 7.48-7.31 (3H, m), 7.20 (1H, d, *J* = 2.9 Hz), 6.69 (1H, s), 6.68 (1H, d, *J* = 2.1 Hz), 6.49 (1H, d, *J* = 2.1 Hz,), 5.40 (2H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.46, 164.11, 163.98, 162.17, 157.81, 135.65, 131.87, 131.20, 130.84, 130.80, 129.07, 128.55, 127.96, 127.76, 126.30, 126.24, 125.09, 106.10, 105.89, 99.03, 93.32, 62.26. Calculated for HRESI-MS $C_{24}H_{16}N_3O_4ClNa$: 468.0727 $[M+Na]^+$. Observed: 468.0735 $[M+Na]^+$.

5-Hydroxy-2-phenyl-7-((1-(*p*-tolyl)-1*H*-1,2,3-triazol-5-yl)methoxy)-4*H*-chromen-4-one (3e): Colour: Pale yellow colour solid. m.p.: 167-169 ºC. Yield: 85%. IR (KBr, ν_{max}, cm^{-1}): 3501, 3075, 2926, 1664, 1622, 1505, 1354, 1163, 821. ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.74 (1H, s), 8.29 (1H, s), 7.90 (2H, dd, *J* = 1.8, 8.2 Hz), 7.55-7.53 (3H, m), 7.15 (4H, dd, *J* = 7.3, 1.9 Hz), 7.03 (1H, s), 6.82 (1H, d, *J* = 2.2 Hz), 6.35 (1H, d, *J* = 2.2 Hz), 5.40 (2H, s), 2.24 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.25, 163.94, 163.70, 157.54, 142.80, 138.2, 131.67, 130.96, 129.07, 128.86, 126.09, 122.55, 105.71, 105.42, 98.29, 93.10, 61.98, 22.44. Calculated for HRESI-MS $C_{25}H_{19}N_3O_4Na$: 448.1273 $[M+Na]^+$. Observed: 448.1283 $[M+Na]^+$.

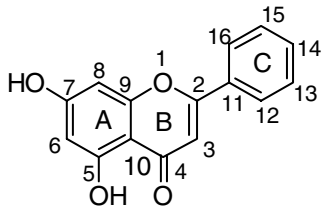
5-Hydroxy-2-phenyl-7-((1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazol-5-yl)methoxy)-4*H*-chromen-4-one (3f): Colour: Pale yellow colour solid. m.p.: 171-172 ºC. Yield: 90%. IR (KBr, ν_{max}, cm^{-1}): 3487, 3109, 2944, 1671, 1623, 1510, 1171, 845, 767. ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.74 (1H, s), 8.09 (1H,s), 7.90 (2H, dd, *J* = 1.8, 8.2 Hz), 7.65 (1H, dd, *J* = 1.8, 8.2 Hz), 7.58-7.52 (5H, m), 7.41 (1H, t, *J* = 8.0 Hz), 6.69 (1H, s), 6.68 (1H, d, *J* = 2.2 Hz), 6.50 (1H, d, *J* = 2.2 Hz), 5.40 (2H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.96, 165.10, 163.42, 161.61, 156.27, 144.40, 137.06, 134.35, 133.19, 125.05, 123.46, 121.83, 105.80, 105.27, 98.35, 91.94, 60.34. Calculated for HRESI-MS $C_{25}H_{16}N_3O_4NaF_3$: 502.0990 $[M+Na]^+$. Observed: 502.0979 $[M+Na]^+$.

5-Hydroxy-7-((1-(4-iodophenyl)-1*H*-1,2,3-triazol-5-yl)methoxy)-2-phenyl-4*H*-chromen-4-one (3g): Colour: Pale yellow-brown colour solid. m.p.: 155-156 ºC. Yield: 89%. IR (KBr, ν_{max}, cm^{-1}): 3462, 3121, 3070, 1653, 1631, 1512, 1184, 824, 683. ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.74 (1H, s), 7.93-7.89 (m, 4H), 7.56-7.53 (4H, m), 7.32 (2H, d, *J* = 8.67), 6.69 (2H, d, *J* = 2.18), 6.53 (1H, d, *J* =2.18), 5.29 (2H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.94, 164.84, 163.08, 161.03, 144.24, 134.57, 133.46, 132.66, 131.66, 129.49, 126.94, 125.65, 106.54, 106.30, 104.15, 102.52, 96.62, 62.05. Calculated for HRESI-MS $C_{24}H_{17}N_3O_4I$: 538.0263 $[M+H]^+$. Observed: 538.0269 $[M+H]^+$.

RESULTS AND DISCUSSION

Chrysin comprises of two fused rings A and B which are joined to phenyl ring C from the second position of the B ring as given underneath as Fig. 1. Chrysin was used as starting material for synthesizing corresponding 1,2,3-triazole derivatives as shown in **Scheme-I** [25,26].

The synthesized compounds were fully characterized by the determination of their physico-chemical properties and spectral characteristics. The chemical structures of the synthesized novel triazole derivatives of chrysin molecules (**3a-g**) were established by ^{1}H & ^{13}C NMR, FT-IR and mass spectral studies. In chrysin, hydroxyl group at 5th position is relatively less reactive than 7th position, due to chelation and strong intramolecular H-bonding between hydroxyl at 5th position and the carbonyl oxygen at 4th position (C-4). The ^{1}H NMR spectrum of compound **2** showed triplet at 2.49 ppm and doublet at 4.61 ppm explained that the propargyl group attachment at 7th position of chrysin it was evidenced by IR band at 3277 cm^{-1} for terminal alkyne group. The appearance of IR stretching 1671-1650 cm^{-1} in the spectral data of synthesized derivatives (**3a-g**) specified the existence of aromatic keto group at C-4 position. The existence of characteristic bands of compounds (**3a-g**) at 3109-3064 and 1631-1607 cm^{-1} indicated the presence of C–H and C=C group in aromatic ring, respectively. The impression of IR absorption band at 3571-3455 cm^{-1} in the spectral data of compounds (**3a-g**) displayed the presence of Ar–OH group on the aromatic ring.



Chrysin (**1**)

Fig. 1

The singlet signals between 7.90 and 8.30 δ ppm in proton NMR spectra is indicative of triazole attached proton of synthesized derivatives. Compounds (**3a-g**) showed singlet at 12.73-12.74 δ ppm due to the existence of OH of Ar–OH. Compounds showed additional peaks at 6.50–7.50 δ ppm due to the existence of additional aromatic ring. Compound **3b** showed two singlets at 3.93, 3.88 δ ppm due to existence of two OCH_3 groups of Ar–OCH_3. Compound **3e** showed singlet at 2.24 δ ppm due to the presence of CH_3 of Ar–CH_3. The ^{13}C NMR spectrum of compounds (**3a-g**) showed peak at 181-183 δ ppm due to the existence of C=O of aromatic ring. The ^{13}C NMR spectral data studies of the triazole derivatives of chrysin molecules (**3a-g**) were found within ± 0.4% of the theoretical results of synthesized compounds. ^{1}H & ^{13}C NMR spectral data of all the individual compounds were in good agreement with the desired structure of the respective compounds.

Biological activity

Antiviral effect against NDV: In view of the outcomes got by Hemagglutination (HA) test on infection titre estimates and side effects in premature chicks, the derivatives displayed critical antiviral activity than that of native molecule. Among the synthesized derivatives **3a-g**, compounds **3a**, **3e**, **3f** and **3g** showed improved antiviral activity (Table-1). All the derivatives showed preferred antiviral action over that of chrysin.

Antiviral effect against BTV: The results revealed that all the synthesized derivatives displayed promising antiviral activity than that of chrysin. Among the synthesized derivatives

TABLE-1
DERIVATIVES (**3a-g**) ANTIVIRAL ACTIVITY AGAINST NEWCASTLE DISEASE VIRUS (NDV) INFECTED EMBRYONATED EGGS OF CHICKS

Derivatives	Number of eggs	Survival				HA test		Titer value
		24 h	48 h	72 h	96 h	Positive	Negative	
3a	5	0 of 5	0 of 5	0 of 5	0 of 5	0	5	1 of 128
3b	5	0 of 5	0 of 5	0 of 5	0 of 5	0	5	1 of 64
3c	5	0 of 5	0 of 5	0 of 5	0 of 5	0	5	1 of 64
3d	5	0 of 5	0 of 5	0 of 5	0 of 5	0	5	1 of 32
3e	5	0 of 5	0 of 5	0 of 5	0 of 5	0	5	1 of 256
3f	5	0 of 5	0 of 5	0 of 5	0 of 5	0	5	1 of 256
3g	5	0 of 5	0 of 5	0 of 5	0 of 5	0	5	1 of 128
Native molecule	5	0 of 5	0 of 5	0 of 5	0 of 5	1	4	1 of 32

TABLE-2
ANTIVIRAL ACTIVITY OF DERIVATIVES (**3a-g**) AGAINST BLUETONGUE VIRUS (BTV) INFECTED CHICKEN EMBRYONATED EGGS

Derivatives	Number of eggs	Survival				HA test		Titer value
		24 h	48 h	72 h	96 h	Positive	Negative	
3a	5	0 of 5	0 of 5	0 of 5	0 of 5	0	5	1 of 128
3b	5	0 of 5	0 of 5	0 of 5	1 of 5	1	4	1 of 64
3c	5	0 of 5	0 of 5	0 of 5	0 of 5	0	5	1 of 256
3d	5	0 of 5	0 of 5	0 of 5	1 of 5	1	4	1 of 128
3e	5	0 of 5	0 of 5	0 of 5	1 of 5	1	4	1 of 64
3f	5	0 of 5	0 of 5	0 of 5	0 of 5	0	5	1 of 128
3g	5	0 of 5	0 of 5	0 of 5	0 of 5	1	4	1 of 32
Native molecule	5	0 of 5	0 of 5	0 of 5	2 of 5	2	3	1of 32

3a-g, compounds **3a**, **3c** and **3f** showed enhanced antiviral activity by disappearing the infection at different titre intervals. Moreover, compounds **3b**, **3d**, **3e** and **3g** additionally displayed promising antiviral action in terms of killing the infection when contrasted with chrysin. All the compounds showed improved antiviral activity than chrysin. Table-2 shows the antiviral characteristics of the synthesized derivatives against blue tongue virus.

***in ovo* antiviral activity against NDV/BTV:** According to the findings of this study, all the synthesized derivatives showed potential activity against both infections, such as blue tongue virus, BHK 21 and newcastle disease virus cell lines. They reduced the cell death caused by newcastle disease and blue tongue viruses in BHK 21 cell lines. Out of all, compounds **3a**, **3e**, **3f** and **3g** showed a noticeable movement against NDV while compounds **3a**, **3b**, **3c**, **3e**, **3f** and **3g** against BTV with greatest cell feasibility likened to the chrysin (Tables 3 and 4).

TABLE-3
in vitro ANTIVIRAL ACTIVITY AGAINST NDV INFECTED BHK 21 CELL LINES FOR DERIVATIVES (**3a-g**)

Derivatives	Newcastle disease virus infected BHK 21 cells (% of live cells)	
	10 µg/mL	20 µg/mL
3a	63	85
3b	60	78
3c	62	80
3d	59	79
3e	64	88
3f	62	87
3g	62	83
Native molecule	45	63

TABLE-4
DERIVATIVES (**3a-g**) *in vitro* ANTIVIRAL ACTIVITY AGAINST BTV INFECTED BHK 21 CELL LINES

Derivatives	Bluetongue virus infected BHK 21 cells (% of live cells)	
	10 µg/mL	20 µg/mL
3a	62	82
3b	54	71
3c	61	81
3d	55	70
3e	59	76
3f	60	81
3g	60	78
Native molecule	41	62

in silico studies

Molecular docking: The structures of HN protein (PDB ID 1USX) and VP7 protein were obtained from the Protein Data Bank (PDB ID 1BVP). Hetero atoms and H_2O molecules were removed from the structures and placed into the MOE working climate, which was followed by protonation and energy minimization using the MMFF94x force field with a cut off value of 0.05. The chemsketch tool was used to create structures and derivatives and the universal force field (UFF) was employed to reduce energy, which was then converted to PDF for docking. For successful docking of structural derivatives and all other places created by superposition of triplets of receptor sites and their ligand atoms, the alpha triangle placement approach is used. A minimum of ten confirmations were generated for each derivative, which were then inspected and rescored. PyMOL Visualizer was used to assess the interactions of ligands with the target protein [27]. The selected effective compounds

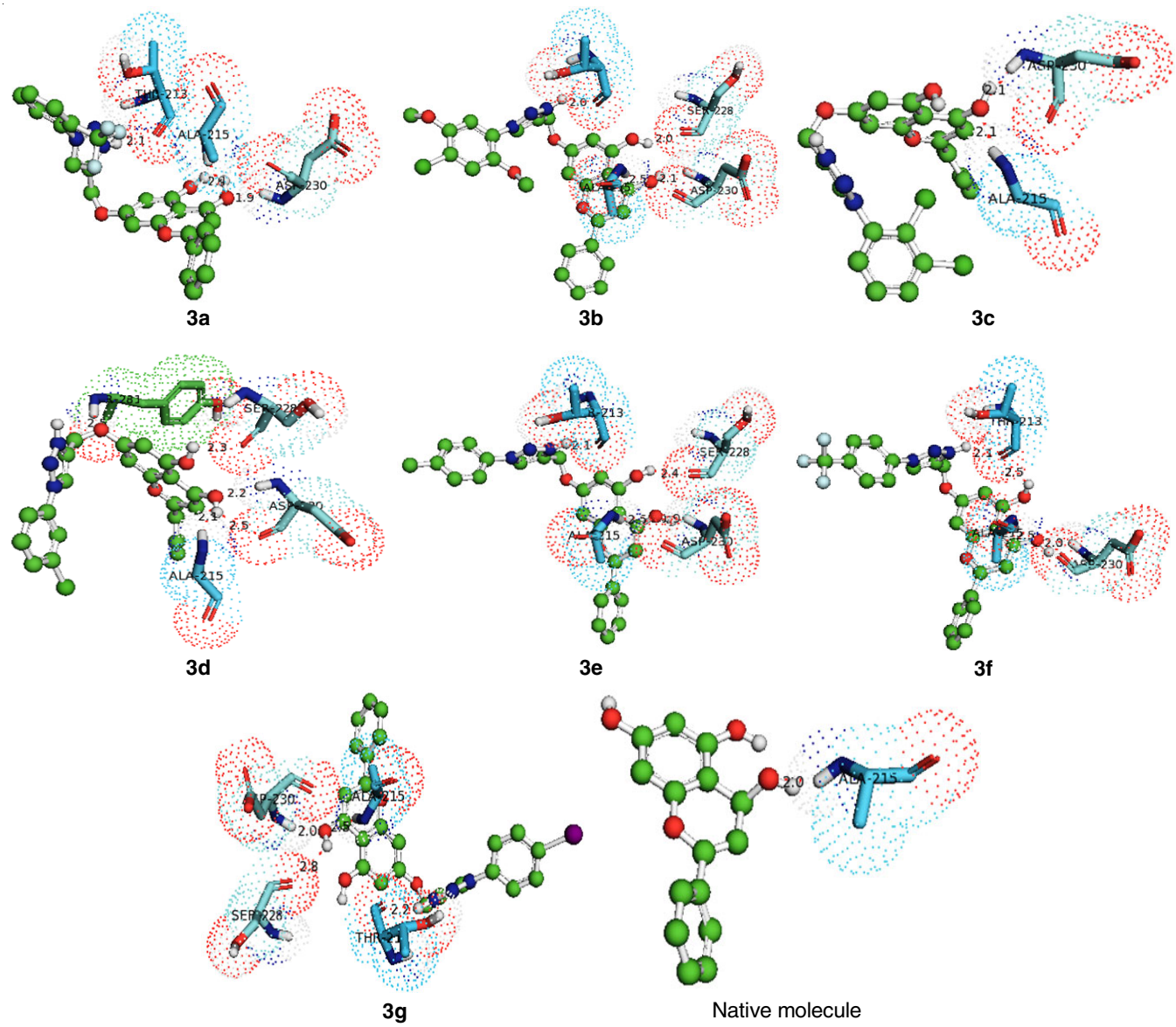


Fig. 2. Bonding interactions between derivatives **3a-g** and native molecule with VP7 of BTV

of each virus protein were produced and assessed for antiviral activity after the molecular docking studies were completed as shown in Fig. 2.

Conclusion

Chrysin was isolated naturally from the hexane extract of *Derris scanden* and triazole derivatives of chrysin were synthesized (**3a-g**). The overall screening revealed that synthesized derivatives are acted as promising antiviral agents when compared with native compound. Among the synthesized compounds, compounds **3a**, **3e**, **3f** and **3g** exhibited prominent activity against NDV whereas **3a**, **3b**, **3c**, **3e**, **3f** and **3g** against BTV with maximum cell viability akin to the rest of the derivatives. As a result, the current study will open up new avenues for the identification of new antiviral medications, with a number of the synthesized derivatives standing out as an interesting therapeutic medication candidate for future optimization and development of prospective antiviral medications.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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