Antioxidant study and Molecular docking of sugar-triazole derivatives

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Abstract. We synthesized a several of sugars-triazole derivatives containing different groups and studied their biological activity with studding molecular docking of these derivatives. To determination antioxidant activity of these derivatives DPPH was used for this purpose. DPPH radicals react with reactive species and scavenging ROS when antioxidant reacted with DPPH radical when donate a hydrogen atom or transfer electron. Molecular docking data of derivatives with spike covid19 (6W41) gives good results can be used in future on how to deal with and treat the virus.

1 Introduction

Oxidation and reduction of molecules occurs in cell organisms. These reactions gives (free radical) chemical species able to independent presence, which contain unpaired one or more unpaired electrons [1]. This electrons available to react with numerous organic materials (biomolecules) in living cell including protein, lipid, nucleic acid and carbohydrate and caused damage of cell [2]. As a result, many dangerous diseases such as cancer are formed [3]. Despite of, also play roles in some pathways, such ROS-mediated reactions shield the cell from oxidative stress and act to stabilize balance reduction and oxidation (redox homeostasis) beside to more important process [4]. But when presence with higher concentration become more dangerous So, living organisms necessary to protect themselves by scavenging ROS and another reactive species via using antioxidants [5]. Antioxidants are any chemicals substance natural or synthetic at low concentrations that inhibit the oxidation of biomolecules. Also antioxidants when react with free radicals can be delay or prevent oxidation process, where's interacted with any steps initiation, propagation, and termination. Antioxidants can be classified according to function to primary and secondary or to enzymatic and non _enzymatic antioxidant [6]. DPPH is one of different analytical methods for estimation of the antioxidant capacity, antioxidant reacted with DPPH radical when donate a hydrogen atom or transfer electron in DPPH radical scavenging [7]. The mechanism action of DPPH [8] show in (Figure 1).

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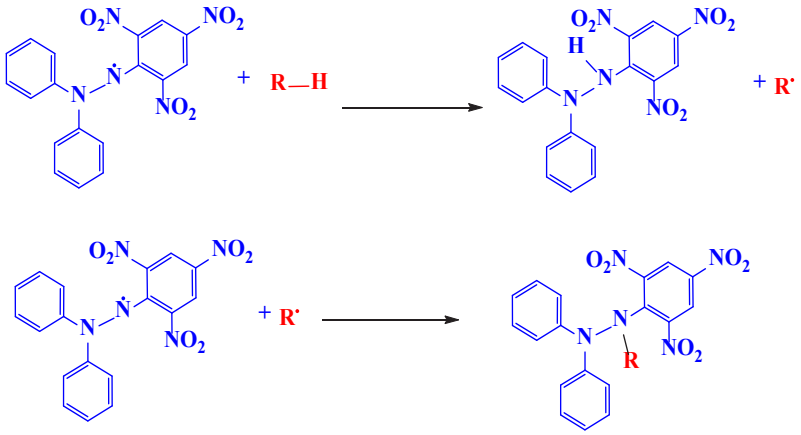

Fig. 1. The mechanism action of DPPH.

Sugars with triazole have wide abroad in biological activities including antibacterial [9], antioxidant and antitumor [10]. Sugars with triazole derivatives were synthesized by click reaction [11]. These derivatives sugars as substrate, gives several advantages biocompatible, low cost, availability, and simple modification methodologies to production derivatives with high biological activity.

2 Methods

All chemicals and of solvents are purchased and used without further purifications are obtained from Sigma Aldrich as analytical grades. The synthesis of these materials have been started with methyl α-D-glucopyranoside which is treated with benz aldehyde dimethyl acetal in DMF to protect the 4, 6- hydroxyls, furthermore, the product was subjected to the reaction with propargyl chloride under phase transfer catalyst to produce methyl 2,3-O-dipropargyl-4,6-benzylideine-α-D-glucopyranoside. The resulted compound was treated with azidobenzyene 4-nitrobenzene azide and 4-chlorobenzene azide under CuAAC 1,3-dipolarcycloaddition to give the triazole derivatives **1**,**2** and **3** respectively. Finally, these compound have been de-protected with acid catalyzed in mixture of chloroform: methanol to furnish compounds **4**, **5** and **6** respectively (Figure 2). All the compounds have been characterized by NMR, FT-IR and mass spectrometry to confirm the structures.

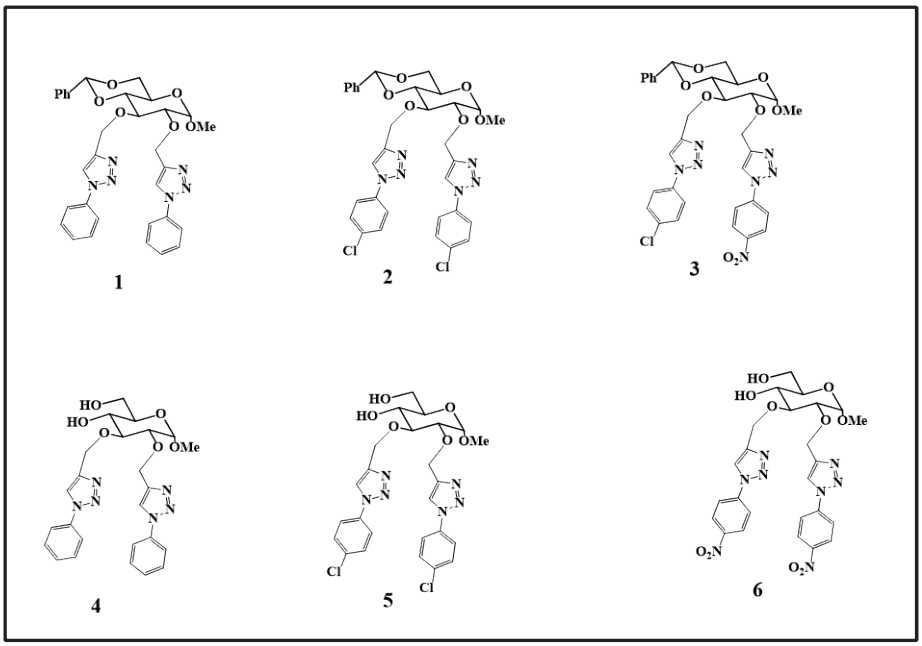

Fig. 2. derivatives of triazole.

3 Results

3.1 Antioxidant study

3.1.1 Preparing standard solutions

Preparing standard solutions with high purity (0.12,0.25,0.5and 1mg) of each sugar derivatives was dissolved in 1mL of methanol to get (0.12,0.25,0.5,1) mg/ml respectively.

3.1.2 Preparing 80mg/ml DPPH reagent

80 mg/mL solution of DPPH reagent preparing by dissolving 8mg of DPPH in 100 ml of methanol.

3.1.3 DPPH Assay to determination antioxidant activity [12]

The radical cation method was modified to estimation the free radical-scavenging effect of Sugars derivatives. DPPH radical cation method was used to determine the scavenging activity, 100 μL DPPH reagent was mixed with 100 μL of sample in a 96-well micro plate and was incubated at room temperature for half hour.After that the absorbance was measured 517 nm using an ELISA reader (TECAN, Gr¨oding, Austria). Methanol(100%) was used as a control [2]. scavenging effect was measured using the following formula:

$$\text{Radical scavenging (\%)}=\frac{\boldsymbol{Acontrol}-Asample}{Acontorl} * X\ 100 \quad (1)$$

$A_{control}$ (absorbance of control) but *A sample* (absorbance of sample)

3.1.4 Antioxidant study

Anti-oxidant study was performed, DPPH was used for this purpose, the new derivatives gives good results as antioxidant by scavenging ROS and another reactive species. From (Table 1) and (Table 2) the sugars –triazole derivatives (**3** and **4**) have a broad spectrum activity in that it. % Scavenging increased with increasing the concentration of these compounds.

Table 1. % Scavenging by derivative **3.**

Sample name	Concentration	Absorbency	Scavenging %
1	0.12 mg/ml	0.3949	62.931
2	0.25 mg/ml	0.3755	64.752
3	0.5 mg/ml	0.3413	67.962
4	1 mg/ml	0.3157	70.365
	control	1.0653	

Table2. Scavenging by derivative **4.**

Sample name	Concentration	Absorbency	Scavenging %
1	0.12 mg/ml	0.4514	56.729
2	0.25 mg/ml	0.3929	62.337
3	0.5 mg/ml	0.3437	67.053
4	1 mg/ml	0.3129	70.006
	control	1.0432	

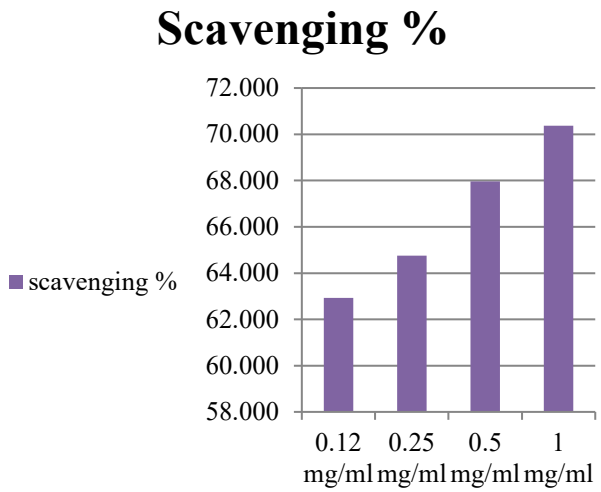

Fig. 1. Relationship between concentration and % scavenging by derivative **3**.

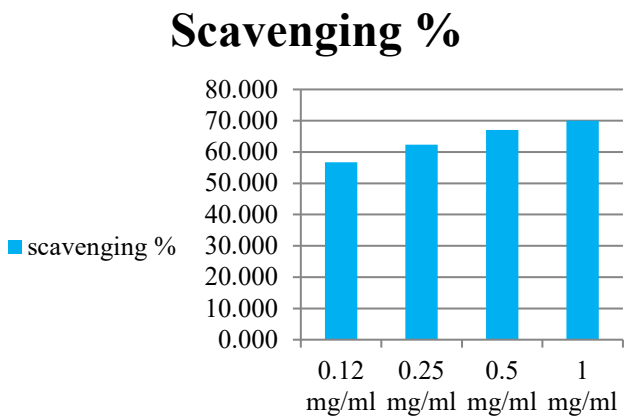

Fig. 2. Relationship between concentration and % scavenging by derivative **4**.

3.1.5 Molecular docking studies [13]

Experimental docking of active and weakly active was done with the help of Glide module of Schrodinger software. The software was installed on Intel core i5-8350U processor. Search the RCSB protein databank to obtain the structure of the target protein. Target ligands were drawn using the chemdraw 22.0.0 program. We have performed docking tests on highly and moderately active molecules.

3.1.6 Ligands Preparation

Chemdraw software was used to draw the ligands in the docking study and then clean up the structure for bond alignment. OPLS3e force field was used (version 2019-1, Schrodinger) to include the ligands and minimize the energy by bond ordering may be assigned with added hydrogens to the ligands, and the 2D structure converted to a 3D for using in docking experiments to choose the best ligand conformations in docking research.

3.1.7 Protein Preparation and Receptor grid generation

Protein Preparation by Schrödinger's wizard (2019-1). Hydrogen and charges altered the protein. Epik produced pH 7.0–2.0 Het states. The protein is pretreated, improved, and tweaked by examining water molecules and other environmental parameters. Only molecules containing heteroatoms remain, and water molecules are essentially were unaffected. Global reduction of this protein was accomplished by the OPLS3 force field. A grid representing the target active site was created using the ligand co-crystallized with the protein (PDB-6W41) for COVID19 studies. The RMSD of the protein after the final docking step with co-crystal ligand in XP mode is 0.46.

Select an inhibitor ligand (X-ray states of the ligand in the protein) to mark receptor grid around the protein (PDB-6W41). Generated grid boxes around the center of ligand and the receptor atoms given a partial atomic charge of 0.25 and a Vander Waal radius of 1.00.

3.1.8 Docking and analysis

Molecular docking employed ligand and protein. XP visualizer (version 2019-1, Schrödinger) analysed the docking study's results. OSIRIS data warrior SMILES-formatted the selected derivatives. Compounds docked by using Schrödinger's Glide module. All docking computations employed XP mode.

3.1.9 Anti COVID

The molecular Operating Environment used to docking simulations for compounds (1,2,3,4,5 and 6) shows the highest binding affinity with spike covid19 (6W41) with very good rmsd and S.

Table 3. Molecular docking data of with spike covid19 (6W41).

Derivatives	Ligand	Receptor	Interaction	Distance	E (kcal/mol
1	5-ring, 5-ring	TRP 436 (C)	pi-pi	3.96	-0.0
2	C 43, 5-ring	TRP 436 (C)	H-pi	3.95	-0.9
3	6-ring CA	PRO 337 (C)	pi-H	3,65	-0.8
4	5-ring, 5-ring	TRP 436 (C)	pi-pi	4.00	-0.0
5	O 14 OG CL 59 O 5-ring, 5-ring	SER 373 (C) O,Val,362(C) TRP,436 (C)	H-donor H-donor pi-pi	2.96 3.59 3.96	-0.8 -0.8 -0.0
6	O 65 N O 66 N	N,ASP,364 (C) N,CYS,336,(C)	H-acceptor H-acceptor	3.21 3.23	-1.2 -1.2

Table 4. Molecular docking data of derivatives (rmsd and S) with spike covid19 (6W41).

Derivatives	rmsd	S
1	2.12	-7.46
2	1.81	-7.18
3	1.51	-7.33
4	1.04	-6.918
5	1.50	-7.71
6	1.72	-7.13

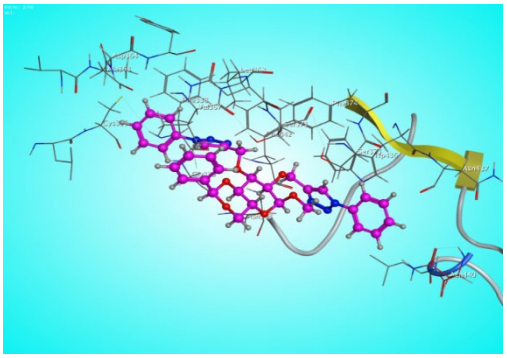

Fig. 3. (3D) Molecular docking of compound **1**.

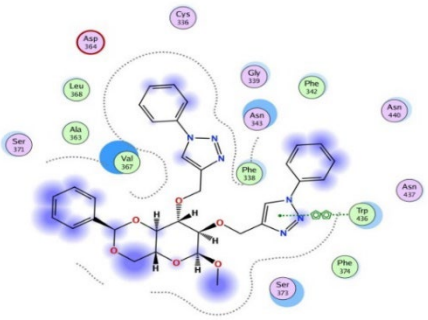

Fig. 4. (2D) Molecular docking of compound **1**.

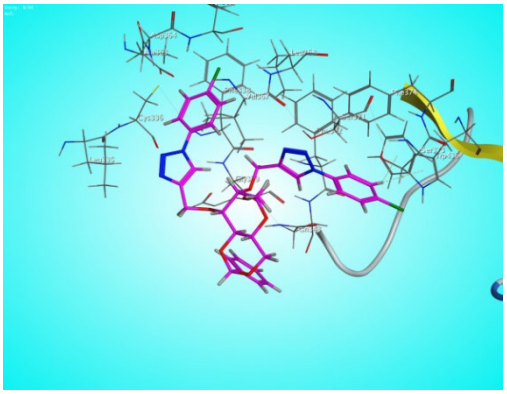

Fig. 5. (3D) Molecular docking of compound 2.

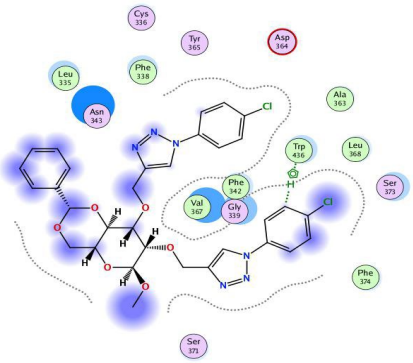

Fig. 6. (2D) Molecular docking of compound 2.

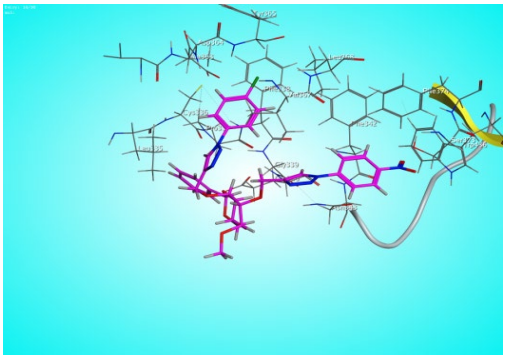

Fig. 7. (3D) Molecular docking of compound **3**.

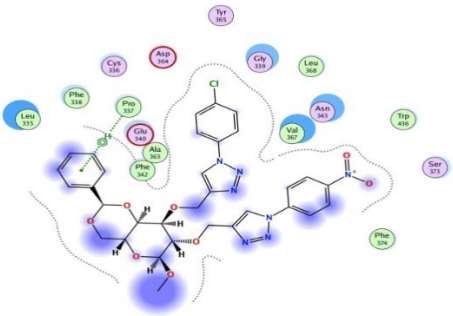

Fig. 8. (2D) Molecular docking of compound **3**.

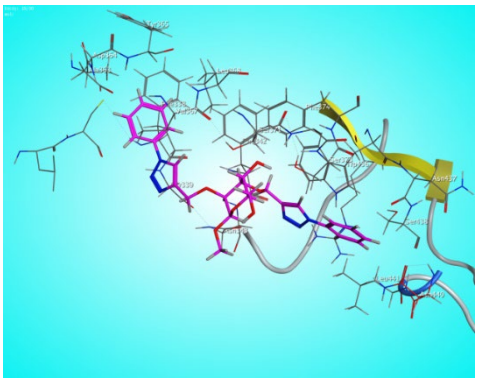

Fig. 9. (3D) Molecular docking of compound **4**

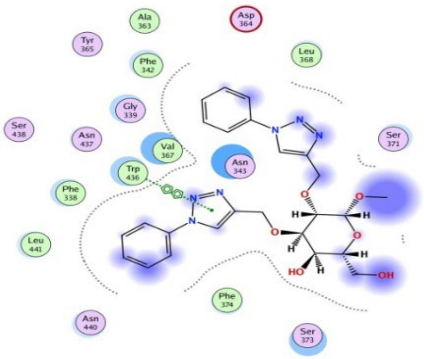

Fig. 10. (2D) Molecular docking of compound **4**

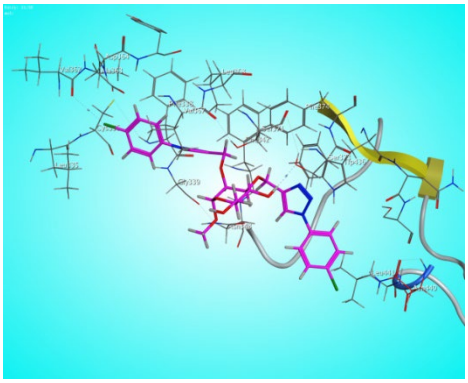

Fig. 11. (3D) Molecular docking of compound **5**.

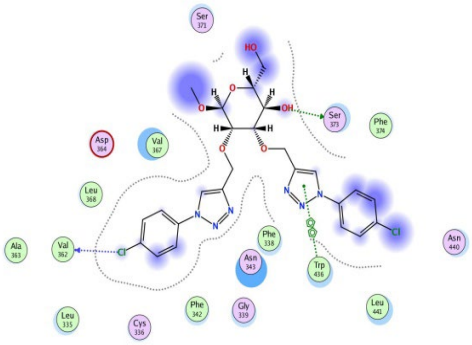

Fig. 12. (2D) Molecular docking of compound **5**.

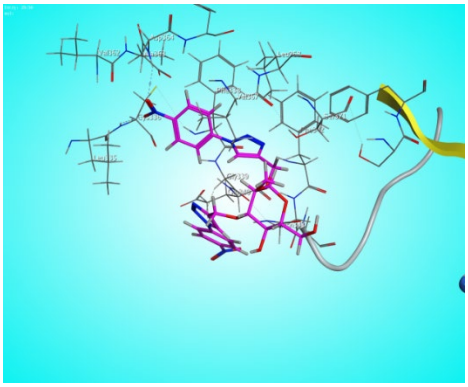

Fig. 13. (3D) Molecular docking of compound **6**.

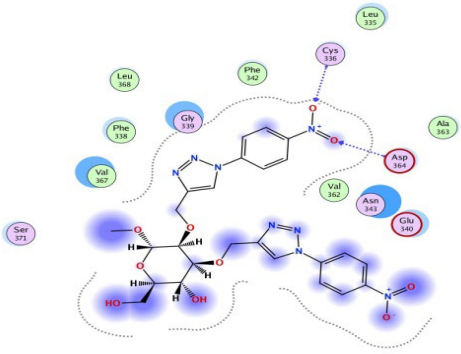

Fig. 14. (2D) Molecular docking of compound **6**.

3.1.10 Ethical disclosures

In this research the procedures followed were following the regulations of the Clinical Research Ethics Committee and the Code of Ethics of the World Medical Association (Declaration of Helsinki) and declare that they have followed the protocols of their work center on the publication of patient data. The authors declare that they have not used any

type of generative artificial intelligence for the writing of this paper.

4 Conclusion

In conclusion, the synthesis of derivatives on glucose with triazole derivatives containing different groups and studied their antioxidant activity with studding molecular docking of these derivatives we can show a broad spectrum activity in that it. % Scavenging increased with increasing the concentration of these compounds. docking simulations for compounds (1,2,3,4,5and 6) shows the highest binding affinity with spike covid19 (6W41) with very good rmsd and S.

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