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Review on Antioxidant Evaluation of 1,2,3-Triazole Derivatives Synthesized by Click Chemistry.

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Abstract

In this review, an important methods for preparing 1,2,3-triazole from a simple reaction is considered within the topic of green chemistry, which is the reaction of the click reaction of the azide–alkyne cycloaddition reaction in the presence of copper as a catalyst. This reaction includes preparation of 1,4-disubstituted 1,2,3-triazoles with a single isomer without the use of high temperature and by using a non-hazardous solvent and with the least possible preparation time. Then the test of 1,2,3-triazole was highlighted as an antioxidant and compared with various standard antioxidants, and it was found to have high efficacy.

Keywords: 1,2,3-triazole, click chemistry, antioxidant.

INTRODUCTION

1- 1,2,3-Triazole derivatives have gained conspicuous significance. Due to the increasing resistance to traditional antibiotics, 1,2,3-Triazoles are an important class of organic compounds due to their large applications in the synthesis of pharmaceuticals, receptors. There is an increasing demand for the preparation of new antimicrobial agents,Due to their broad range of biological activities {1}.In synthetic organic chemistry, and also because of the pharmacological properties shown by some of its derivatives, the 1,2,3-triazole ring system has been the subject of considerable study. We agreed to investigate the 1,2,3-triazole ring system as a new scaffold for cannabinoid ligands in this context.{2} 1,2,3-triazoles derived from monosaccharides have been synthesized and their glycosidase-inhibiting activities have been established, such as alpha-glucosidase, isomaltase, amyloglucosidase and β-glucosidase, sweet almond β-glucosidase and alpha-glucosidase yeast{3}.After the discovery of the Cu(I) catalyzed azide-alkyne 1,3-dipolar cyclo addition reaction, 1,2,3-Triazole modified carbohydrates became readily accessible and soon became a popular class of unnatural sugars. {4,5}. 1,2,3-triazole is a stable liquid (melting point 296 K) at room temperature, while other heterocyclic compounds with contiguous atoms of nitrogen (pyrazole, 1,2,4-triazole or tetrazole) are solid. It is a synthetic molecule and its derivatives are commonly used in pharmacology and food-farming

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as building blocks for many complex chemical products, the solid phase of 1,2,3-triazole was investigated by Goddard, by X-ray diffraction per single crystal. Tested gas-phase tautomerism by microwave spectroscopy, Microwave spectroscopy reveals that the 1,2,3-triazole gasphase consists of the tautomer T-2H, with a relatively low approximate T-1H:T-2H ratio (10-3 at room temperature) {6}.1,2,3-Triazole a significant class of heterocyclic compounds that have wide applications such as fungicides, plant growth regulators, dyes, and corrosion inhibitors are triazoles and their derivatives. Over the years, 1,2,3-Triazoles have also attracted continued interest from organic and medical scientists due to their wide range of biological activities, such as antibacterial, antiallergic, 1,2,3-Triazole as anti-inflammatory, immunosuppressive, anabolic and contraceptive agents, steroidal compounds are used widely. They have also been used for treating breast and prostate cancer and against leishmaniasis {7-10}.1,2,3-Triazole derivative antifungal properties contributing to the invention of fluconazole, variconazole, albaconazole and itraconazole{11}. In the design of ligands for metal complexes, organic molecular catalysts, medicinal compounds, and supramolecular architectures, 1,4-disubstituted 1,2,3-triazoles, readily accessible through copper(I)-catalyzed Huisgen cycloaddition, have been widely exploited {12}.

2- Click chemistry is a newer method for the synthesis of drug like Molecules that can improve the drug development process by using a Practical and accurate responses are few. The 1,2,3-triazole catalyzed by Cu(I) The reaction between azides and terminal alkynes has evolved to form Due to their reliability, specificity, the gold standard of click chemistry, and Biocompatibility.[13] The click reaction is a variation of the Huisgen 1,3-dipolar cycloaddition reaction between terminal acetylenes and triazole-building azides, one of the powerful reactions described by Kolb et al in 2001[14][15]for the development of carbon-heteroatom-carbon bonds in an aqueous environment.[16] A modular synthetic approach towards the assembly of new molecular entities is click chemistry. The broad reach of CuAAC is clearly demonstrated by its usage in various fields of life and material sciences, such as drug development, bioconjugation, polymer and materials science[17]And similar ones Additional examples of the use of CuAAC are areas including supramolecular chemistry, DNA labeling and oligonucleotide synthesis,[assembly of glyco-clusters and glycodendrimers,[preparation of stationary stages for HPLC column, development of microcontact printing, conjugation of molecular cargos to the phospholipid head group, and construction of bolaamphi-philic structures.[18] The benefits of the "click" catalyzed Cu(I) reaction are that (i)it is regioselective, while the non-catalyzed Huisgen reaction loses regioselectivity, generating both the 1,4- and 1,5-disubstituted isomers, (ii)it continues. It meets the criteria of 'green chemistry' at a milder temperature than the non-catalyzed reaction (iii)to the degree that it can occur in an aqueous or alcoholic medium,(iv)Sharpless and Fokin's recorded catalyst is simple and inexpensive; it consists of $CuSO_4 \cdot 5H_2O$ + sodium ascorbate, the latter reagent being perfect for Cu(II) to Cu(I) reduction, but not Cu(0).[19] By means of the dipolar1,3-cycload reaction of organic azides to γ-lactones containing terminal

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triple bonds, the synthesis of new 1,2,3-triazoles has been modified. Previously, the synthesized compounds in literature were nondescript. The optimum reaction conditions were ensured by high yields of the final products.[20] Total substitution-easy synthesis of completely substitution- A very simple catalytic system consisting of copper(I) oxide and methanol under atmospheric conditions has been successfully introduced from organic halides, terminal alkynes, and sodium azide with an alkynyl moiety of 1,2,3-triazoles at 5-position. For the various disciplines concerned with click chemistry, this finding will be of great interest.[21] 1,2,3-Triazoles were prepared under solventless conditions at good to moderate yields by cycloading alkyl azides on enol ethers. The reaction may have access to ring-fused triazoles that are inaccessible and easily scalable by azide-alkyne cycloadditions. 1,2,3-triazole products have properties that can be quickly derivatized.[22] 1,2,3- Triazoles are one of the most significant five-membered het-containing nitrogen— In pharmaceuticals, supramolecular chemistry, organic synthesis, chemical biology and industry, eurocycles have a broad range of applications.[23]

3- Antioxidants Our body's biochemical processes, like aerobic metabolism and inflammatory responses, as well as environmental exposure, result in unstable and highly reactive free radicals(are molecules, ions or atoms with their outermost electron shell, with unpaired electrons[24} such as reactive oxygen (ROS) including hydroxyl radical (OH) ,hydrogen peroxide(H2O2),superoxide anion(O2) and nitrogen (RNS) species including nitric oxide{25} .In causing oxidative stress and harming most biomolecules, including lipids, proteins, nucleic acids (DNA, RNA), ageing, and carbohydrates, both play an important role.{26}.The results of cellular and tissue damage are now related to many chronic disorders, including Alzheimer's ddiseas{27}, cancer ,diabetes, rheumatoid arthritis {28} and ,neurodegenerative disorder {29} , And other illnesses that arise through The Free Radicals' violent reactivity {30} .While ROS plays a significant biological role in cell signaling, homeostasis and micro-organism defense, an imbalance between the production of ROS and the removal of ROS through the antioxidant protection system of the cells. Oxidative stress and diverse pathological disorders can be caused by endogenous antioxidants, enzymes, dietary antioxidants, and metal-binding proteins {31}. Antioxidants are essential compounds that minimize or neutralize free radicals thereby protecting cells from oxidative harm {32} A variety of cellular protection mechanisms have developed to counteract ROS accumulation, including enzymatic scavengers antioxidants such as catalase (CAT), glutathione peroxidase (GPx) and superoxide dismutase (SOD), as well as non-enzymatic antioxidants such as glutathione, ascorbic acid (vitamin C); regulating the balance between antioxidants and ROS, ubiquinole, carotenoids, tocopherols and polyphenolic components {33,34} furthermore The frequency of degenerative diseases like cancer, CVD and aging is decreased by flavonoids.. Synthetic antioxidants such as butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), tert-butylhydroquinone (TBHQ) and propyl gallate (PG) have been commonly used in the food and pharmaceutical industries to

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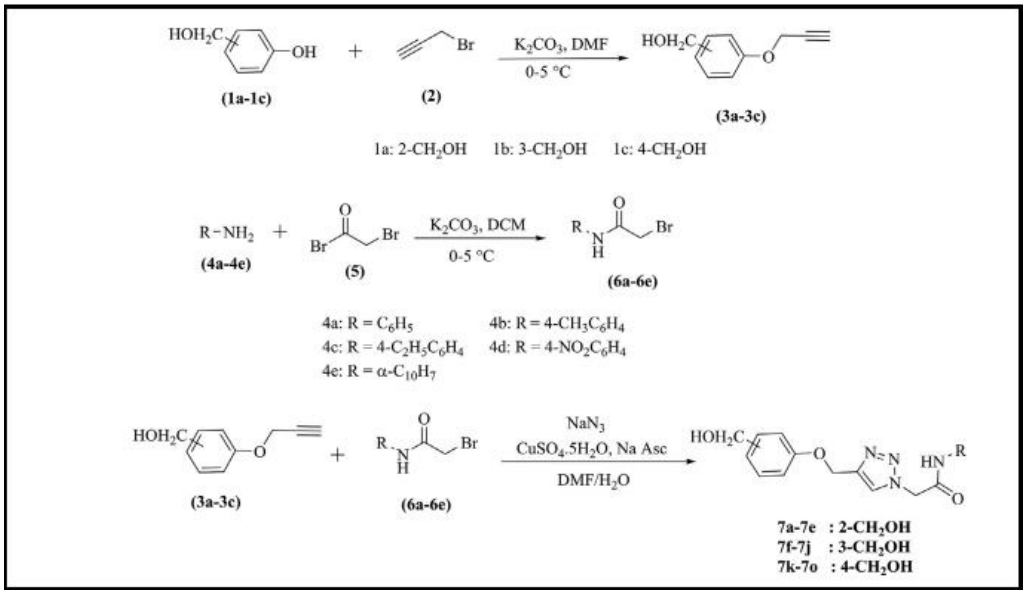
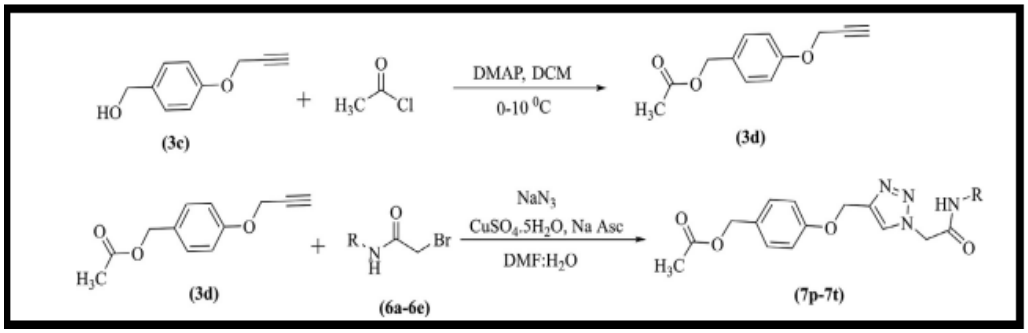
protect products from oxidative degradation(Any health risks, including cancer and carcinogenesis) and enhance shelf-life{35,36}

EXPERIMENTAL SECTION

C.P. Kaushika et al {37} were synthesized a series of amide-linked 1,4-disubstituted 1,2,3-triazoles by click chemistry approach in order to explore antioxidant agents with improved potency. FTIR, 1H NMR, 13C NMR spectroscopy and HRMS were used to characterize the structure of synthesized triazoles. The antioxidant activity was evaluated using stable free radical 1,1-diphenyl-2-picrylhydrazyl assay (DPPH) and it was noticed that compound 7d has shown the best value in comparison to ascorbic acid.



Scheme 1. Synthesis of amide linked 1,4-distributed 1,2,3-triazole.



Scheme 2. Synthesis of ester-amide linked 1,4-disubstited 1,2,3-triazoles.

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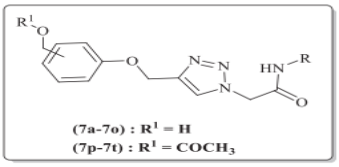
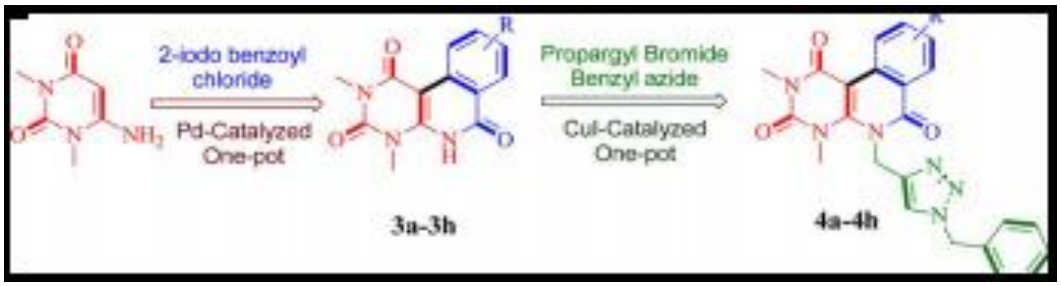
Table 1

Inhibition of DPPH radical by synthesized compounds.



Compounds	IC_{50} (µg/mL) ± SD	Compounds	IC_{50} (µg/mL) ± SD
7a	2.65 ± 0.79	7k	3.2 ± 0.35
7b	3.63 ± 0.98	7l	3.08 ± 0.88
7c	4.27 ± 0.08	7m	3.69 ± 0.67
7d	**1.61 ± 0.23**	7n	2.26 ± 0.04
7e	3.73 ± 0.59	7o	3.37 ± 0.53
7f	3.34 ± 0.89	7p	2.62 ± 0.39
7g	3.83 ± 0.15	7q	6.04 ± 1.03
7h	5.55 ± 0.71	7r	5.69 ± 1.21
7i	2.92 ± 0.47	7s	4.45 ± 0.09
7j	4.3 ± 0.69	7t	5.52 ± 0.79
Ascorbic acid	1.41 ± 0.06	Ascorbic acid	1.41 ± 0.06

Sirassu Narsimha etal {38} In the one-pot process, a sequence of novel pyrimido[4,5-c] isoquinolines (3a-3h) and 1,2,3-triazole-coupled pyrimido[4,5-c]isoquinolines (4a-4h) were synthesized with good to excellent yields. In vitro analysis of antioxidant activity indicated that 4d and 4c compounds displayed potent antioxidant activity relative to the regular Trolox drug with IC50 values of 6.02: 0.6 and 8.27: 1.0 µM,



Scheme 3. Synthesis of 1,2,3-triazole-coupled pyrimido[4,5-c]isoquinolines

Table 2. Antioxidant activity of **3a-3h** and **4a-4h** by DPPH method.

Compound	IC_{50} in µM	Compound	IC_{50} in µM
3a	56.09 ± 1.3	4a	39.66 ± 1.2
3b	27.29 ± 1.0	4b	19.28 ± 1.6
3c	17.94 ± 1.1	4c	8.27 ± 1.0
3d	10.22 ± 0.8	4d	6.02 ± 0.6
3e	40.03 ± 1.9	4e	18.62 ± 1.2
3f	46.11 ± 1.4	4f	12.18 ± 0.9
3g	38.03 ± 0.9	4g	23.17 ± 1.0
3h	51.19 ± 1.3	4h	37.26 ± 1.6
Trolox	11.73 ± 1.5	Trolox	11.73 ± 1.5
Ascorbic acid	3.34 ± 1.8	Ascorbic acid	3.34 ± 1.8

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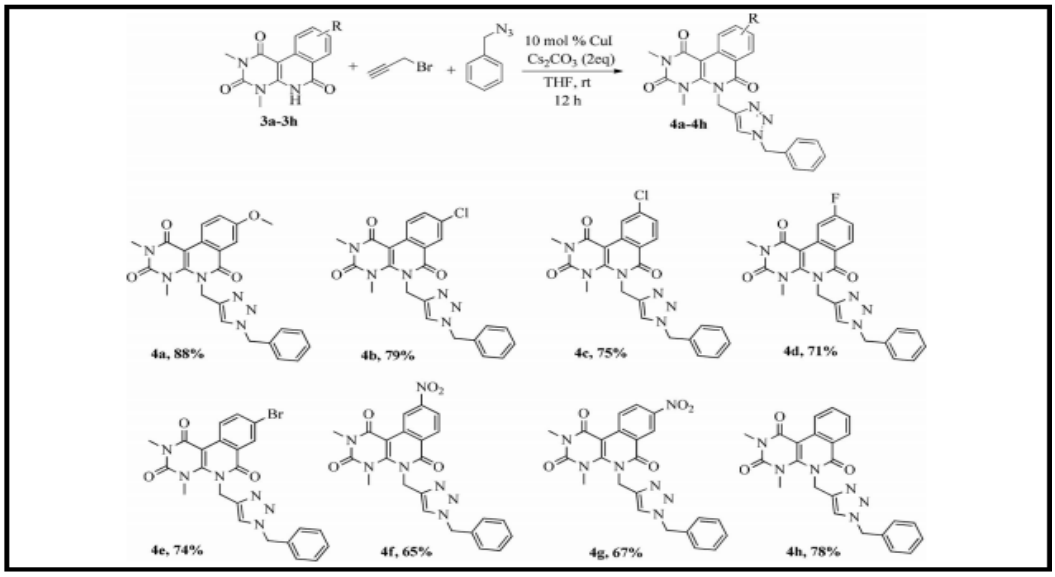
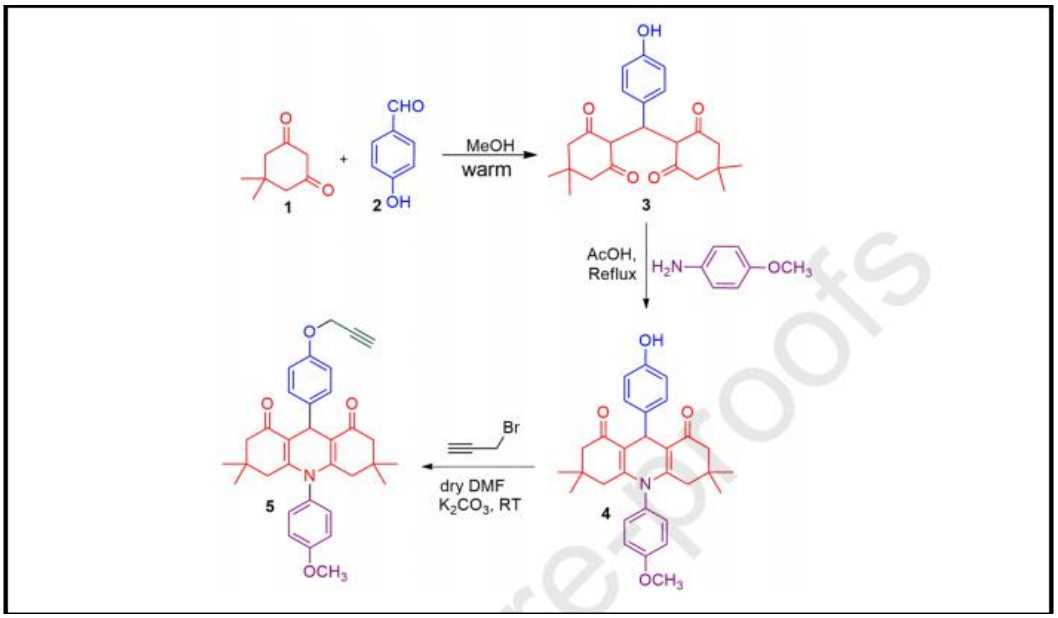


Scheme 4. One-pot synthesis of 1,4-disubstituted 1,2,3-triazole hybrids (**4a-h**).a Note:THF,tetrahydrofuran. a. Isolated yield.

Rajesh Raju et al {39} With good yields using intermolecular Cu(I) catalyzed azide and alkyne click reaction, an expedient regioselectivesynthesis of novel mono, C2-symmetric bis-triazole and acridinedione bridged macromolecules was achieved. In three good yielding steps starting from dimedone, O-propargyl acridinedione synthesis was achieved, whereas symmetrical aliphatic and aryl bis-azides were extracted from dimedone. Macromolecules 9,12, and 13 have been shown significant anti-oxidant properties comparable to that of standard ascorbic acid.



Scheme 5.synthesis of dipolarophile.

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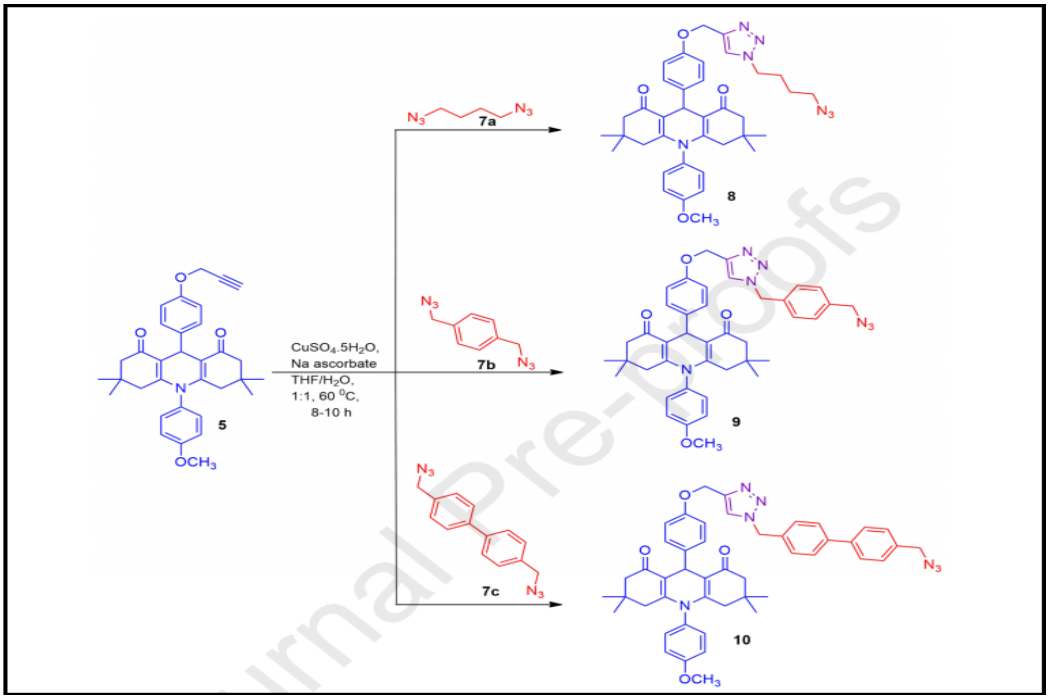
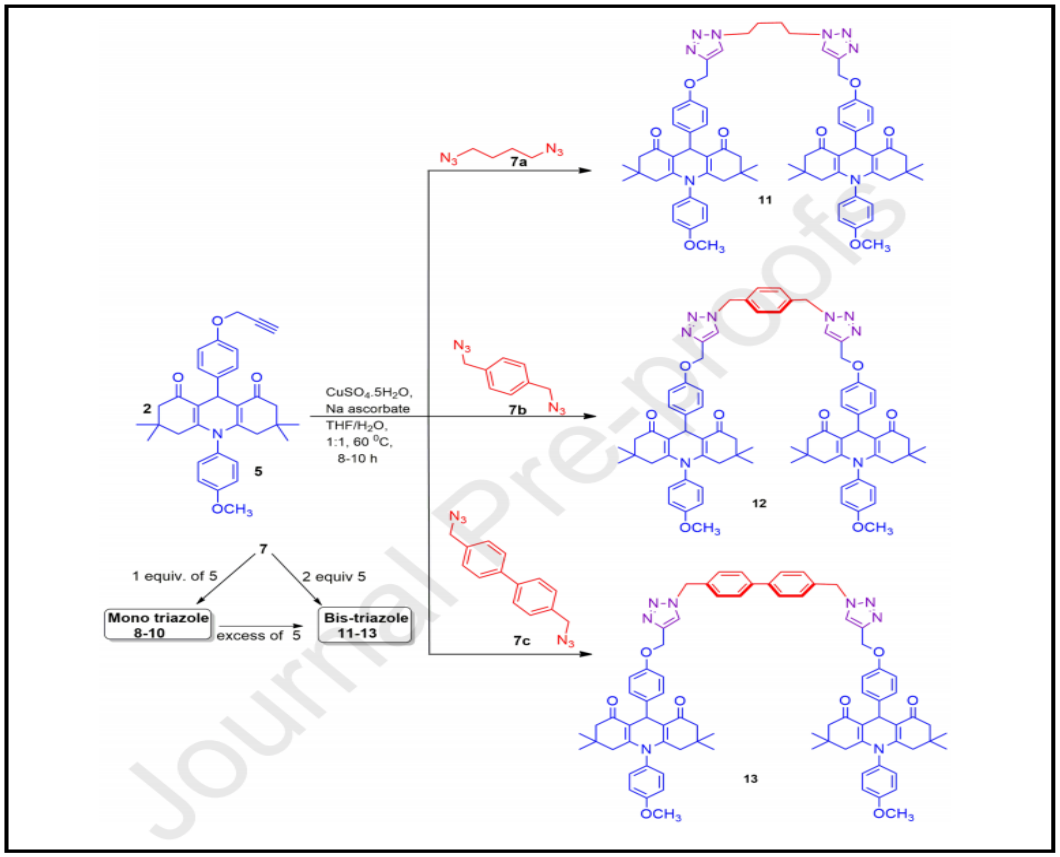


Scheme 6. Synthesis of mono 1,2,3-triazole.



Scheme 7. Synthesis of C2-symmetric macromolecules.

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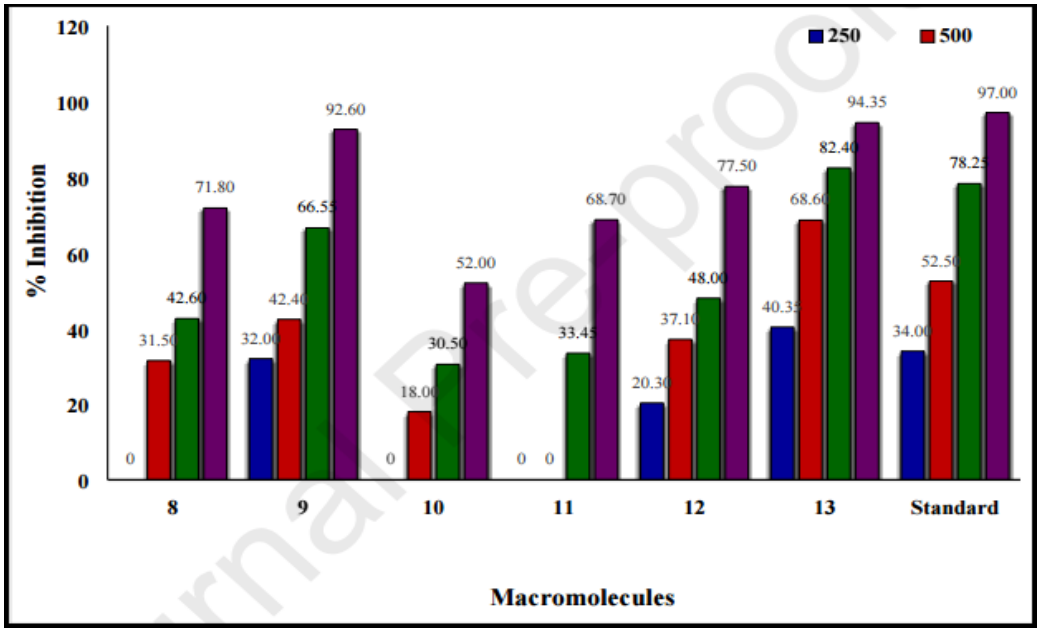
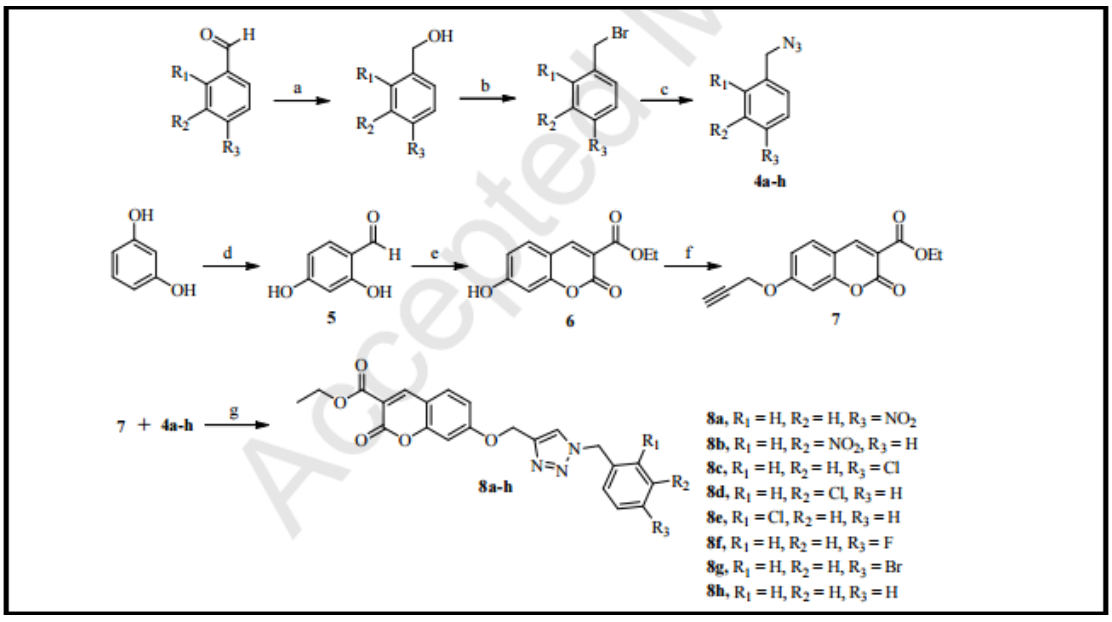


Figure 1. Antioxidant activity of synthesized macromolecules versus ascorbic acid as a standard by DPPHscaveging method.

Mubarak H. Shaikha etal {40} Click chemistry was used to synthesize a sequence of novel ethyl-7-((1-(benzyl)-1H-1,2,3-triazol-4-yl)methoxy)-2-oxo-2Hchromene-3-carboxylates. Antioxidant activity was also measured for the coumarin-based triazole derivatives and compound 8a was found to be a potent antioxidant relative to the standard medication. .



Scheme 8. Synthetic route for target compounds **8a-h**

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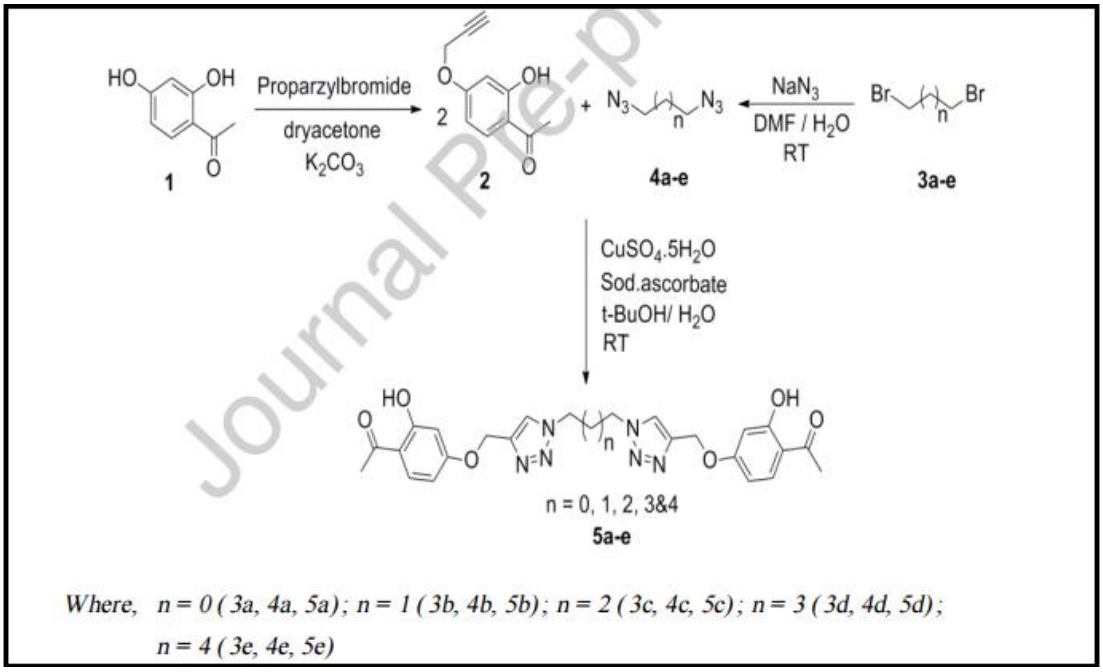
Table 3 In vitro antimicrobial and antioxidant evaluation of coumarrin based triazoles and their precursor molecules.

Entry	MIC Values in μg/mL					Antioxidant activity (IC_{50}μg/mL)
	CA	*FO*	*AF*	*AN*	*CN*	DPPH scavenging activity
6	100	150	NA	NA	NA	58.21
7	NA	NA	175	NA	175	17.06
8a	50	100	125	50	150	15.20
8b	50	100	125	150	150	16.89
8c	25	50	25	100	150	16.00
8d	25	25	100	25	100	15.99
8e	25	12.5	150	175	150	15.29
8f	12.5	50	50	25	100	16.95
8g	50	50	125	125	150	29.12
8h	25	50	50	100	150	40.36
Miconazole	25	25	12.5	25	25	NT
Fluconazole	12.5	6.25	6.25	12.5	6.25	NT
BHT	NT	NT	NT	NT	NT	16.47

I. Vania et al {41} For the microwave-assisted synthesis of dimers of 1,2,3-triazole-benzofuran carrying alkyl spacer derivatives 7a-j by intermediate, bis-1,2,3-triazole carrying alkyl spacer compounds 5a-e, an effective and convenient approach was established with excellent yields. Through the DPPH process, compound 7j showed strong antioxidant activity..



Scheme 9. Synthesis of 1,1-((((1,1-(n-alkyl)bis(1H-1,2,3-triazole-4,1-diyl))bis(methylene))bis(oxy))bis(2-hydroxy-4,1-phenylene))diethanone (**5a-e**).

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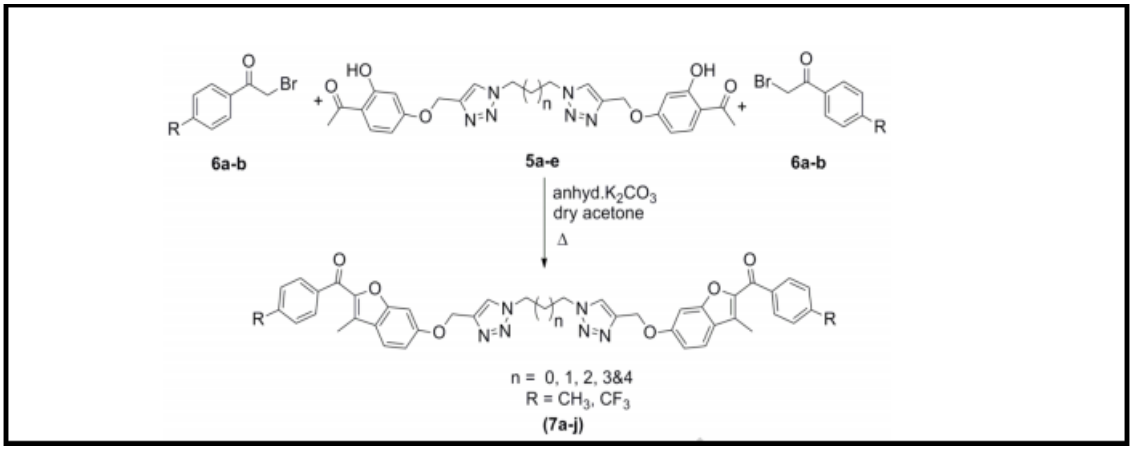

Scheme 10. Synthesis of (6,6-(((1,1-(propane-1,3-diyl)bis(1H-1,2,3-triazole-4,1-diyl))bis(methylene))bis(oxy))bis(3-methylbenzofuran-6,2-diyl))bis(4-substituedphenylmethanone)(**7a-j**).

Table 4 . Antioxidant activity of synthesized compound **7a-j**

Compound	*Scavenging activity (IC_{50} µg/ mL)*	
	DPPH	*H_2O_2*
7a	*20.12 ± 0.54*	*18.26 ± 0.28*
7b	*22.95 ± 0.51*	*23.95 ± 0.84*
7c	**13.04 ± 0.81**	*19.65 ± 1.14*
7d	*19.22 ± 0.34*	*13.87 ± 1.11*
7e	*21.62 ± 0.57*	*14.25 ± 0.38*
7f	*21.68 ± 1.02*	*16.03 ± 0.71*
7g	**11.56 ± 1.09**	*21.69 ± 0.65*
7h	*17.62 ± 0.24*	**11.32 ± 0.52**
7i	*20.01 ± 0.31*	*18.32 ± 0.11*
7j	**11.09 ± 0.30**	*22.92 ± 0.38*
*AA**	*15.54 ± 0.67*	*14.65 ± 0.76*
BHT†	*17.22 ± 0.21*	*16.21 ± 0.14*

**Ascorbic acid; †Butylated Hydroxy Toluene.*

Jalal Hasan Mohammed, etal [42] Synthesis and antioxidant activity Eight new compounds (1,2,3,4,5,6,7,8) were produced from the interaction of a number of aromatic and aliphatic compounds with propargyl bromide to subsequently prepare alkynes; alkynes are reacted with organic azide to form eight new 1,2,3-triazole compounds (9,10,11,12,13,14,15,16) by click reaction Using copper as a catalyst After that, an antioxidant was performed for prepared triazole, radical scavenging activity of DPPH and the best result values were 76.54+-1.9 for compound 9 Compared to the standard model ascorbic acid concentration values of 86.03+-4.02 at 200 mg/ml**.**

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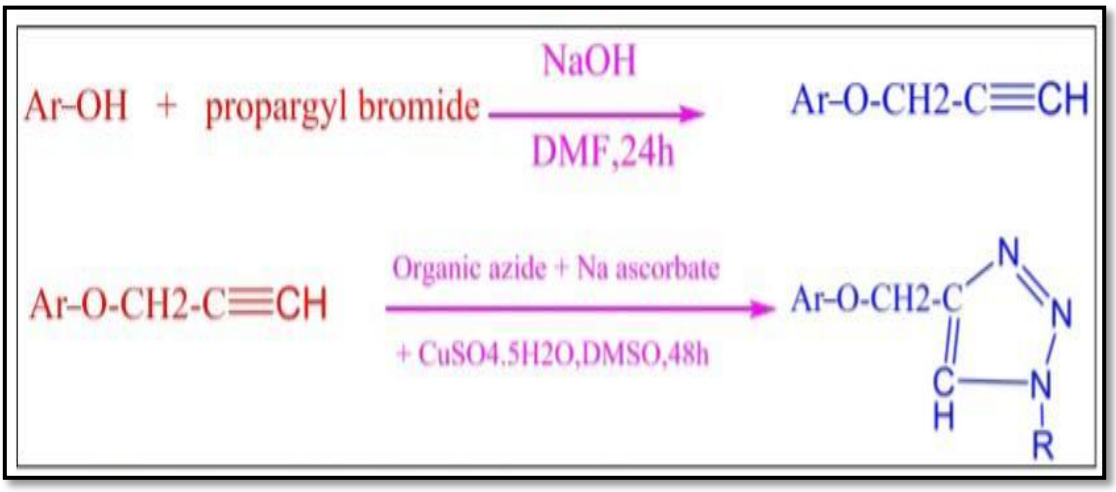
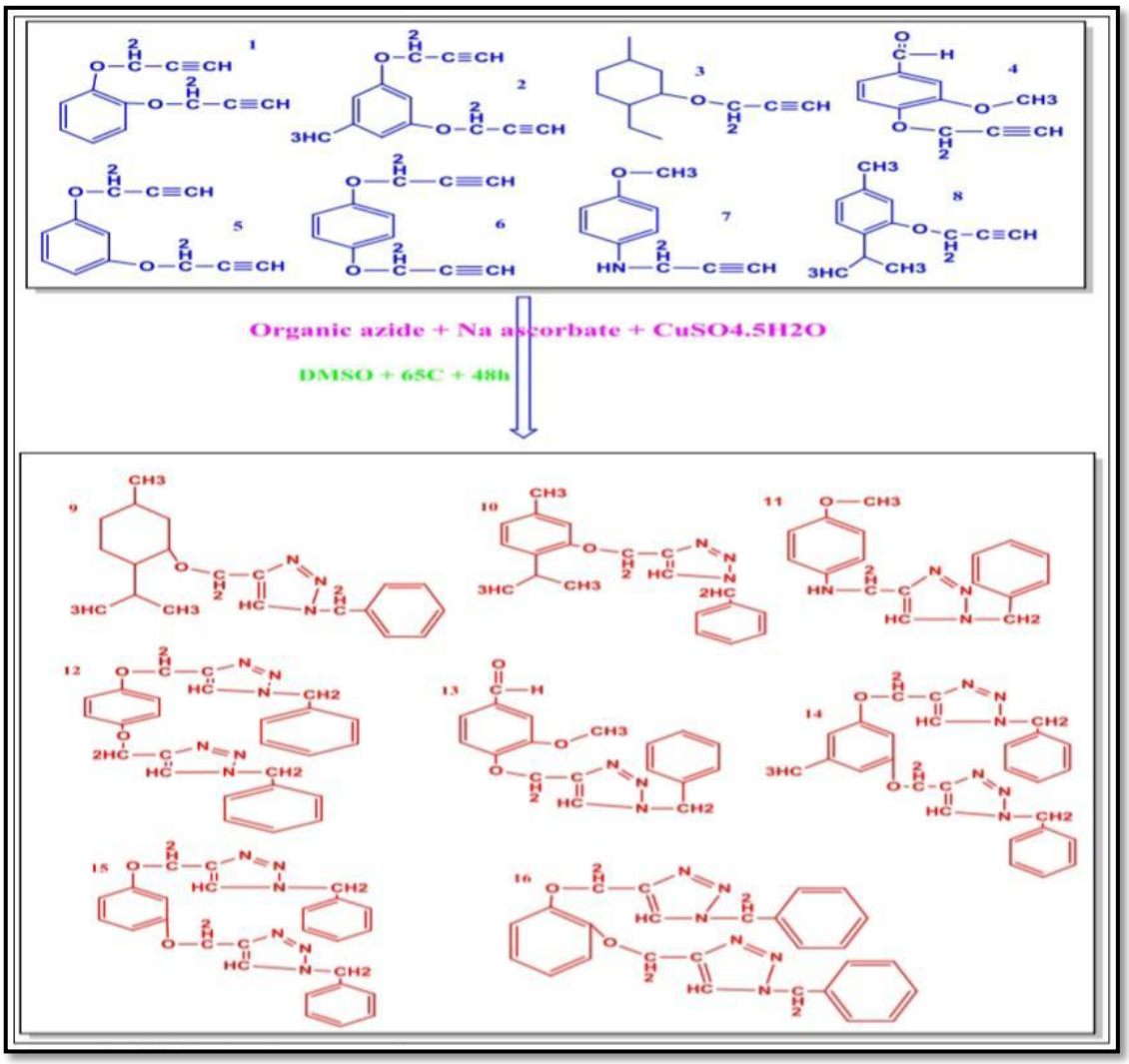


Scheme 11: The alkyne and triazole synthesis equation



Scheme 12: Click chemistry equation

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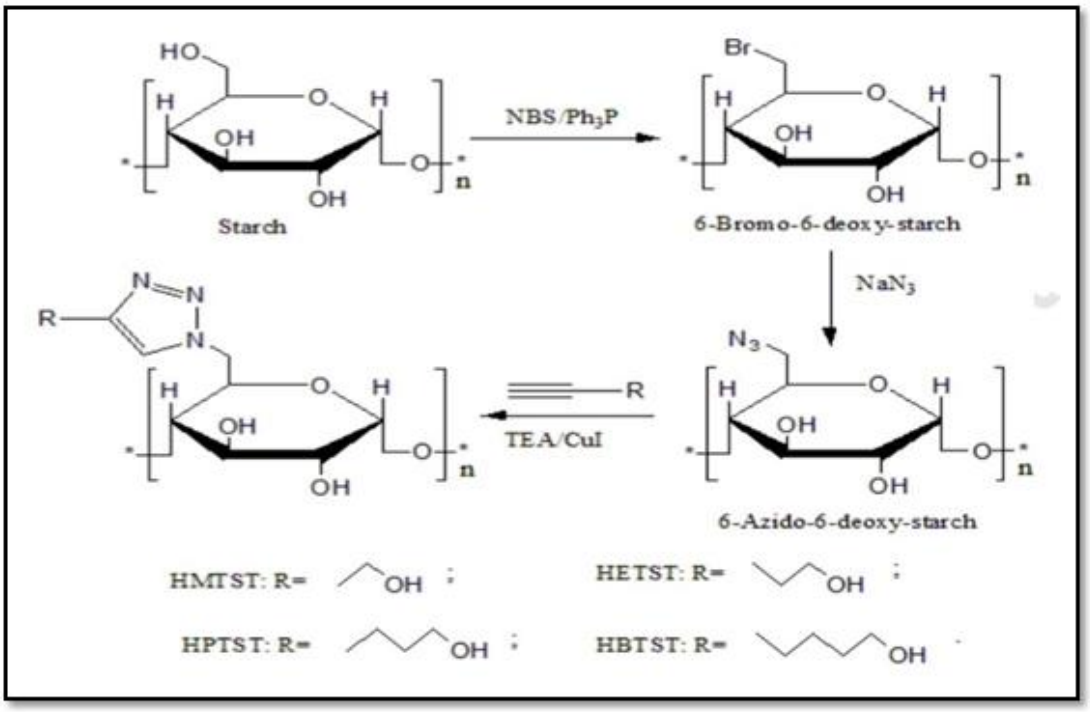
Sample	Concentration Mg/ml				
	200	100	50	25	12.5
Ascorbic acid	86.03+-4.02	74.07+-1.0	57.60+-2.2	39.00+-1.7	22.90+-1.8
15	73.57+-1.0	63.70+-1.2	54.48+-1.3	40.43+-4.0	17.63+-4.1
14	54.59+-1.1	43.79+-0.9	21.34+-4.0	17.40+-2.4	20.60+-3.7
16	74.92+-1.1	62.15+-3.3	51.16+-1.7	28.70+-4.2	14.93+-0.5
11	41.05+-1.5	27.24+-0.7	25.42+-1.6	16.90+-3.0	15.78+-0.5
10	50.50+-5.2	40.28+-2.0	35.19+-4.6	17.67+-3.0	17.40+-2.4
12	65.20+-2.3	52.43+-2.9	44.10+-0.8	30.56+-2.7	17.63+-2.0
9	76.54+-1.9	62.08+-0.5	52.74+-1.8	39.62+-2.3	27.70+-0.7
13	44.02+-1.8	34.92+-1.1	20.10+-2.2	17.21+-1.7	14.54+-1.5

.Table 5. of scavenging activity assay by DPPH of all compound*s*

Wenqiang Tan, etal [43] Synthesis and antioxidant properties of novel 1,2,3-triazole-linked starch derivatives via click chemistry. The antioxidant properties of novel 1,2,3-triazole-linked starch derivatives against hydroxyl-radical, DPPH-radical and superoxide-radical were evaluated in vitro. in order to evaluate their antioxidant activity,The modern amphiprotic starch derivatives have shown substantial improvement over starch**.**



Scheme 13. Synthetic routes for starch derivatives.

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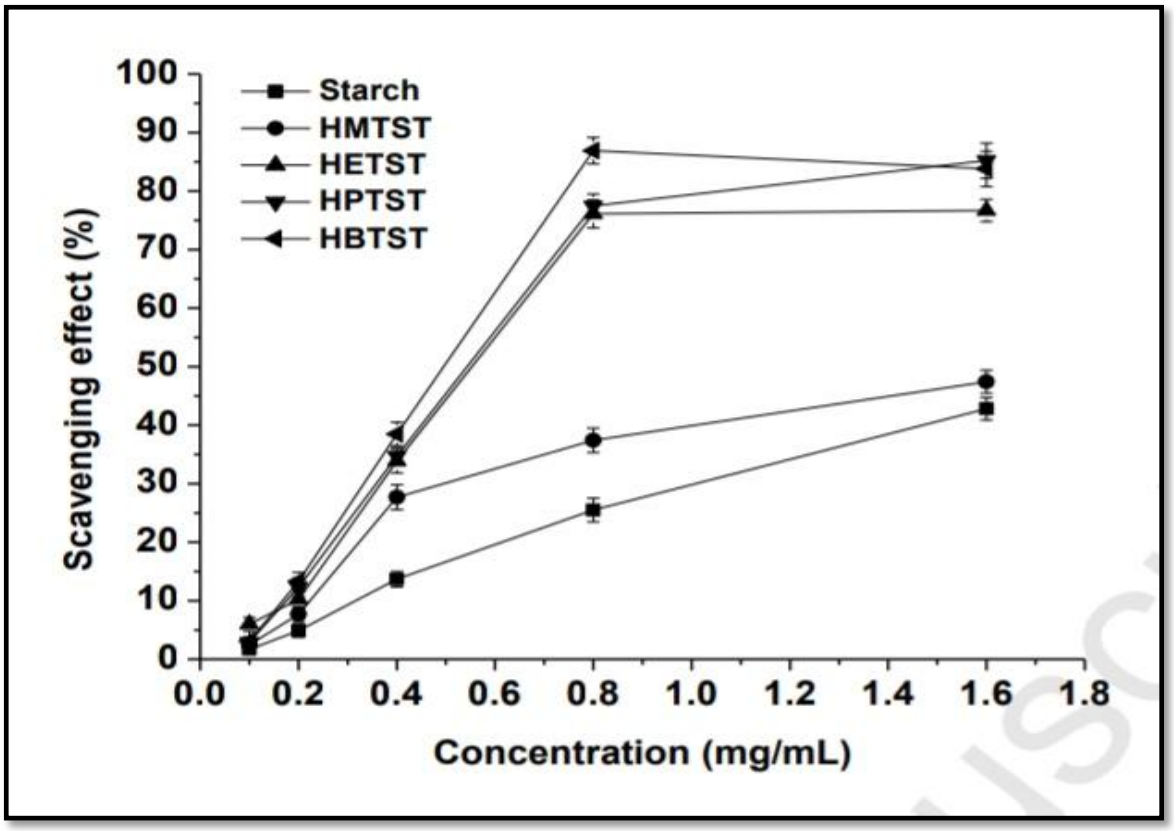

Fig. 2. Hydroxyl-radical scavenging ability of starch and starch derivatives.

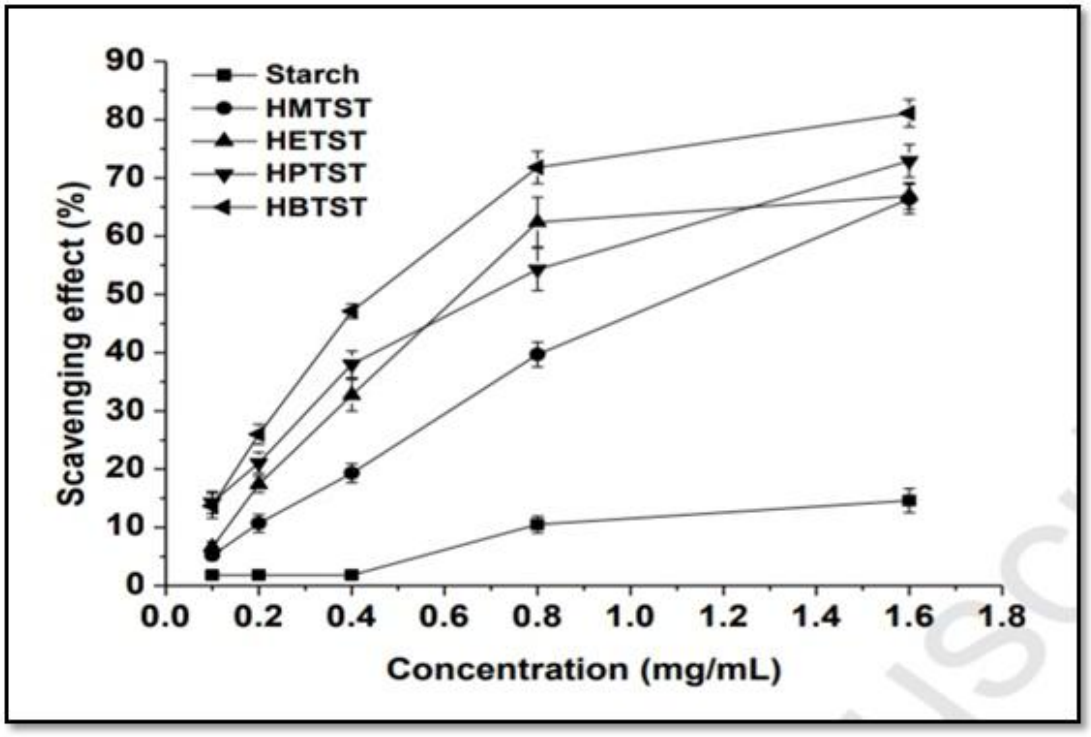

Fig. 3. DPPH-radical scavenging ability of starch and starch derivatives.

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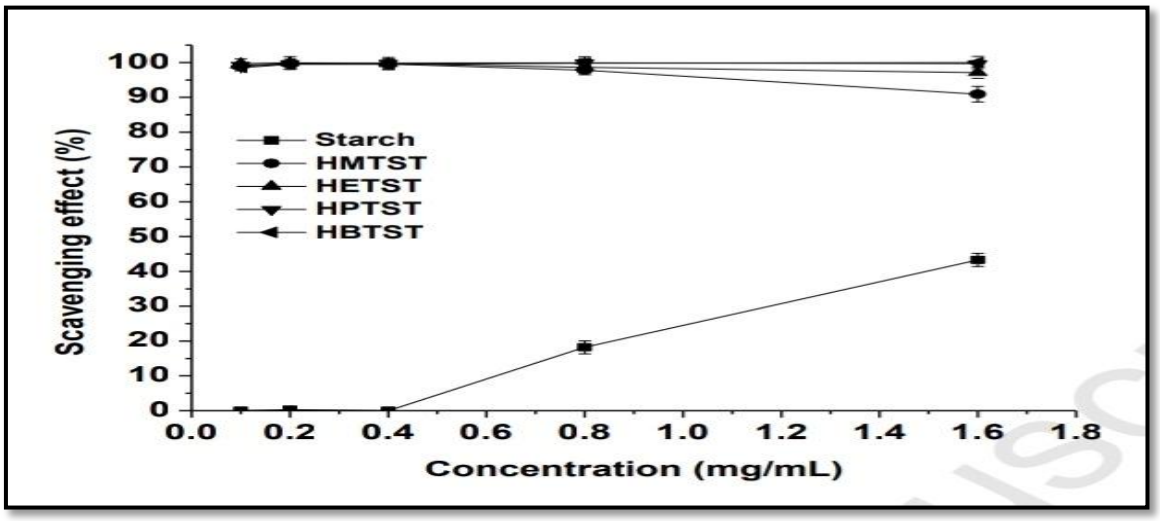

Fig 4. Superoxide-radical scavenging ability of starch and starch derivatives.

Maria C. F. Dias, etal [44] The twenty-six 1,2,3-triazole-benzophenone derivatives series were obtained in two phases, 4,4'-dihydroxybenzophenone (1a) and 2,4-dihydroxybenzophenone (1b) propargylated, affording the alkynes bis(4-(prop-2-yn-1-yloxy))benzophenone (2a) and (2-hydroxy-4-(prop-2-yn-1 yloxy))benzophenone (2b), respectively. These derivatives were provided with yields ranging from 35 to 95 percent by the copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction between the 2a/2b compounds and several benzyl azides. The compounds were evaluated with regard to their photoprotective, antioxidant, and cytotoxicity in vitro.

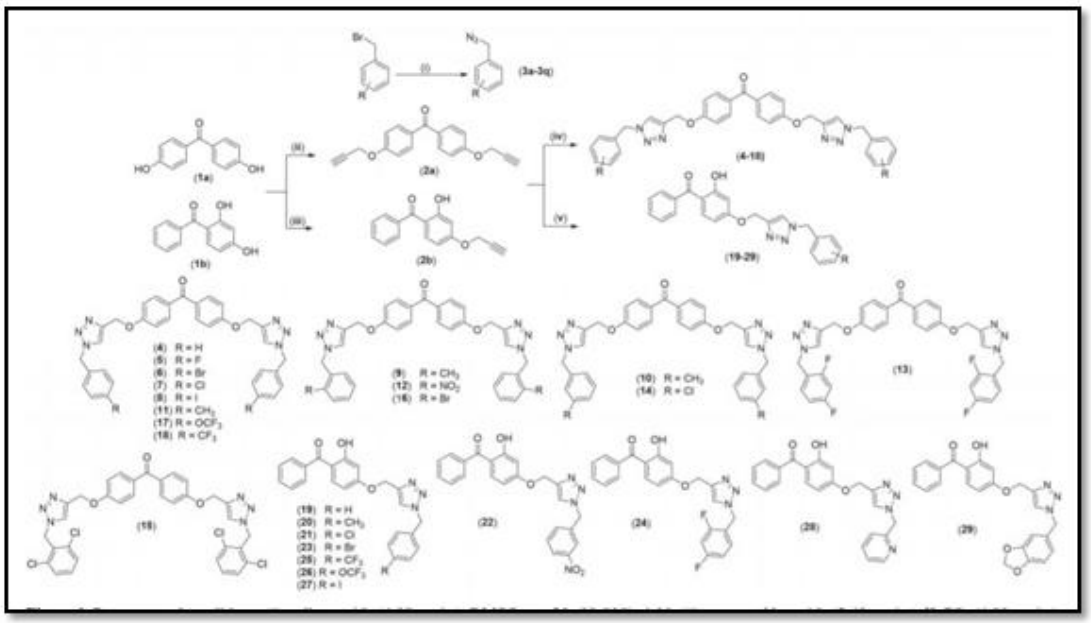

Figure 5. Reagents and conditions: (i) sodium azide (4.00 equiv.), DMSO, r.t., 2 h, 80-90% yield; (ii) propargyl bromide (2.40 equiv.), K2CO3 (4.00 equiv.), Acetone, reflux, 24 h, 83%; (iii) propargyl bromide (1.20 equiv.), K2CO3 (2.00 equiv.), acetone, reflux, 24 h, 61%; (iv) CuSO4·5H2O (0.400 equiv.), sodium Ascorbate

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(0.800 equiv.), DCM/H2O (1:1 v/v), r.t., 6 h, 42-70%; (v) CuSO4·5H2O (0.200 equiv.), sodium ascorbate (0.400 equiv.), DCM/H2O (1:1 v/v), r.t., 6 h, 35-95%.

Table 6. *Trolox equivalent antioxidant capacity (TEAC) for 1,2,3-triazole Benzophenone derivatives. The TEAC is related to the antioxidant capacity of a given substance, as compared to the standard Trolox*

Compound	TEAC / (mmol L^{-1} g^{-1})	
	After 2 h	After 4 h
1b	5.96 ± 0.769^{a}	7.57 ± 1.635^{a}
2a	4.77 ± 0.092^{b}	$4.39 \pm 0.404^{a,b}$
2b	22.61 ± 0.743^{c}	22.91 ± 0.267^{c}
5	2.16 ± 0.462^{d}	$2.24 \pm 0.195^{b,d}$
8	$7.12 \pm 0.109^{a,b,e}$	$8.16 \pm 0.528^{a,e}$
13	$7.64 \pm 0.350^{a,e,f}$	$9.51 \pm 0.460^{a,e,f}$
17	$2.09 \pm 0.063^{d,g}$	$2.42 \pm 0.705^{b,d,g}$
18	$7.68 \pm 0.816^{a,e,f,h}$	$9.44 \pm 0.081^{a,e,f,h}$
19	$22.16 \pm 0.644^{c,i}$	$23.70 \pm 1.29^{c,i}$
20	$2.41 \pm 0.823^{b,d,g,j}$	$8.34 \pm 1.12^{a,e,f,h,j}$
21	$4.53 \pm 1.065^{b,d,e,g,j,k}$	$4.96 \pm 0.359^{a,b,d,e,g,k}$
22	$5.71 \pm 0.453^{a,b,e,f,h,k,l}$	13.89 ± 1.373^{l}
23	$8.68 \pm 0.007^{a,e,f,h,m}$	19.27 ± 0.995^{m}
24	$4.72 \pm 0.091^{b,d,e,j,k,l,n}$	$7.66 \pm 0.777^{e,f,h,j,k,o}$
26	$8.10 \pm 0.176^{a,e,f,h,l,m,o}$	$11.05 \pm 0.601^{e,f,h,j,k,p}$
27	$7.90 \pm 0.776^{a,e,f,h,l,m,o,p}$	$8.43 \pm 0.243^{a,e,f,h,j,o,p,q}$
28	$3.67 \pm 0.264^{b,d,g,k,l,n,q}$	$4.15 \pm 0.567^{b,d,g,k,r}$

Different letters were used to compare the significance between compounds at the same time ($p < 0.05$ according to ANOVA followed by Tukey post-test).

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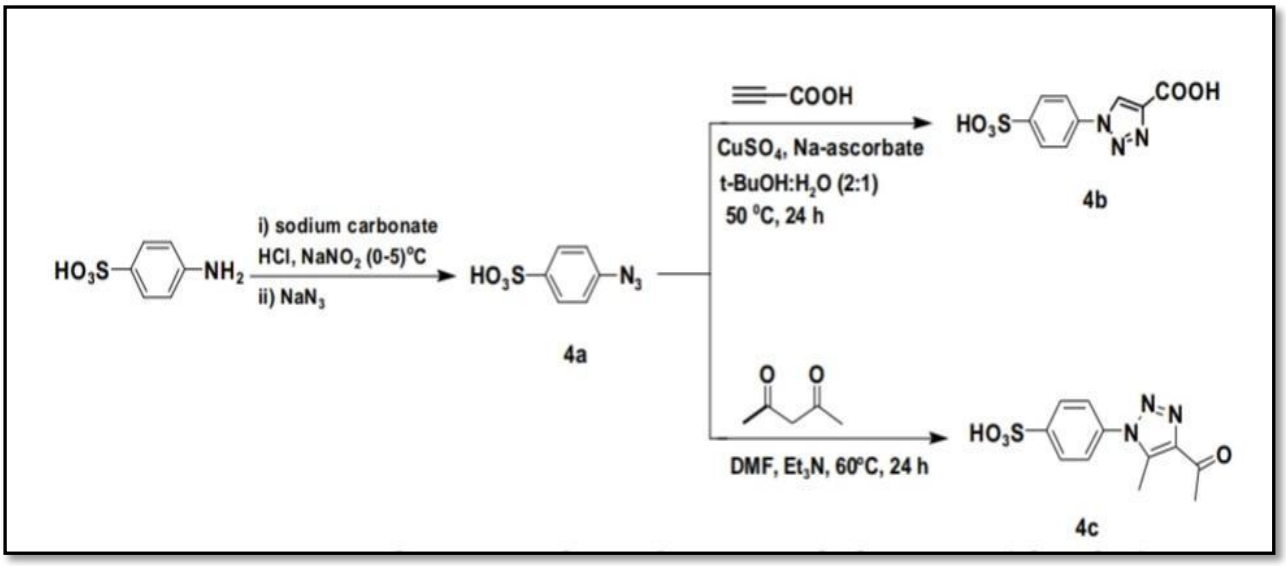
Riyadh J. Nahi, etal [45] Synthesis of 1,3-oxazepine derivatives via a cycloaddition reaction with maleic and phthalic anhydrides. In addition, two new 1,2,3-traizole derivatives were synthesized in a simple synthetic acid moiety containing benzene sulfonic acid 1,3-dipolarcycloaddition p-azidobenzene sulfonic acid reaction with propriolic acid and acetylacetone in the presence of different conditions. FT-IT, 1H-NMR, 13C-NMR and mass spectroscopies have confirmed the compounds. In addition, all the heterocyclic compounds synthesized showed promising antioxidant activity against DPPH.



.(c4 dna b4) sevitavired elzoairt-1,2,3 fo sisehtnyS :14 emehcS

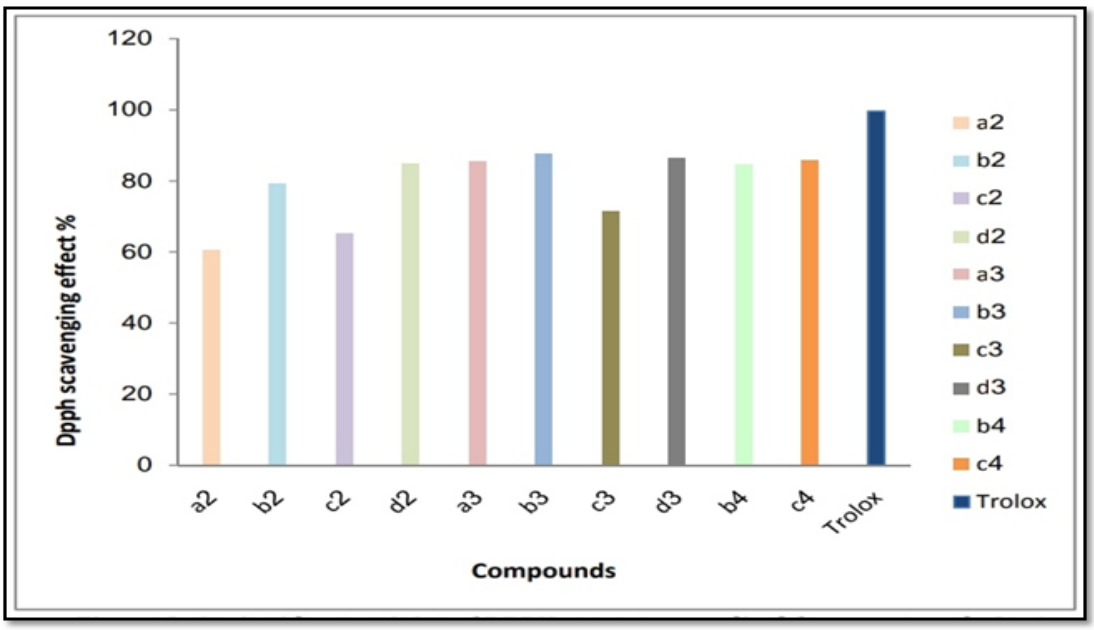


Figure 5: Antioxidant activity of DPPH scavenger radical for compounds 2a-4c.

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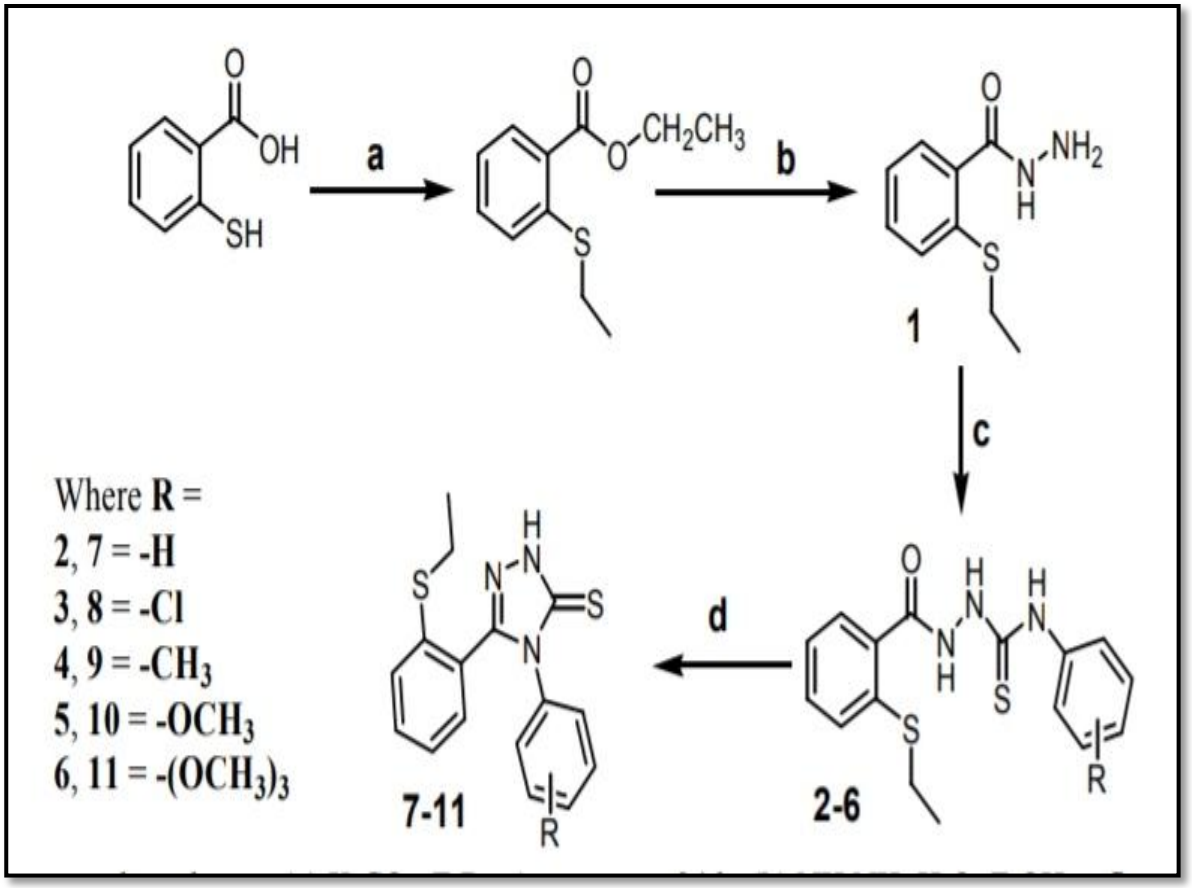
Nafal Nazarbahjat, etal [46] New thiosemicarbazide 2-6 derivatives were synthesized by reacting with different aryl isothiocyanates to 2-(ethylsulfanyl)benzohydrazide. Compounds 7-11 containing a 1,2,4-triazole ring were formed by the cyclisation of compounds 2-6 under reflux conditions in a simple medium (aqueous NaOH, 4 N). The synthesized compounds were all Screened for their behavior with antioxidants. In a 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay, compounds 2, 3, and 7 showed improved radical scavenging, with IC50 values of 1.08, 0.22 and 0.74 μg/mL, respectively,Compared to gallic acid (IC50, 1.2 μg/mL).In a ferric reducing antioxidant strength (FRAP) assay (3054 μM/100 g), compound 3 also reported superior results compared to those of ascorbic acid (1207 μM/100 g).



Scheme 15. Synthetic pathway of thiosemicarbazides and 1,2,4-triazolethiones.

Reagents and conditions: (a) K2CO3, EtBr, Acetone, r.t, 24 h; (b) NH2NH2·H2O, EtOH, reflux, 24 h; (c) EtOH, arylisothiocyanates, reflux, 1–4 h; (d) 4N NaOH, reflux 3 h.

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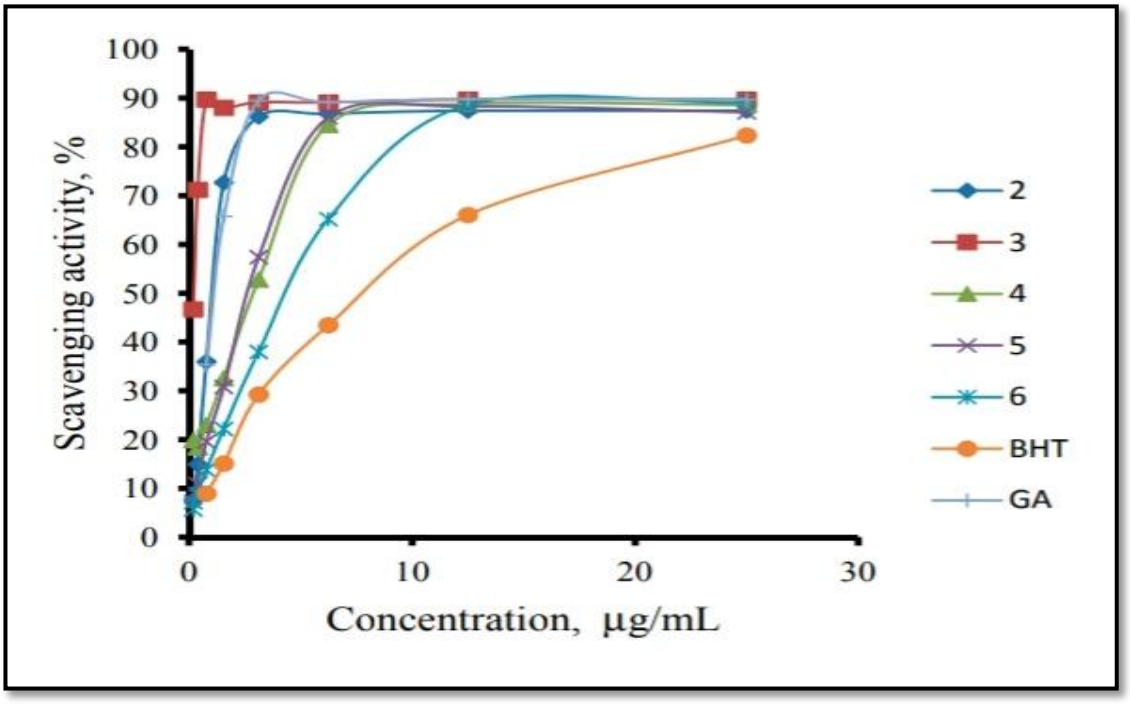

Figure 6. Scavenging activity of compounds 2–6 on DPPH radical.

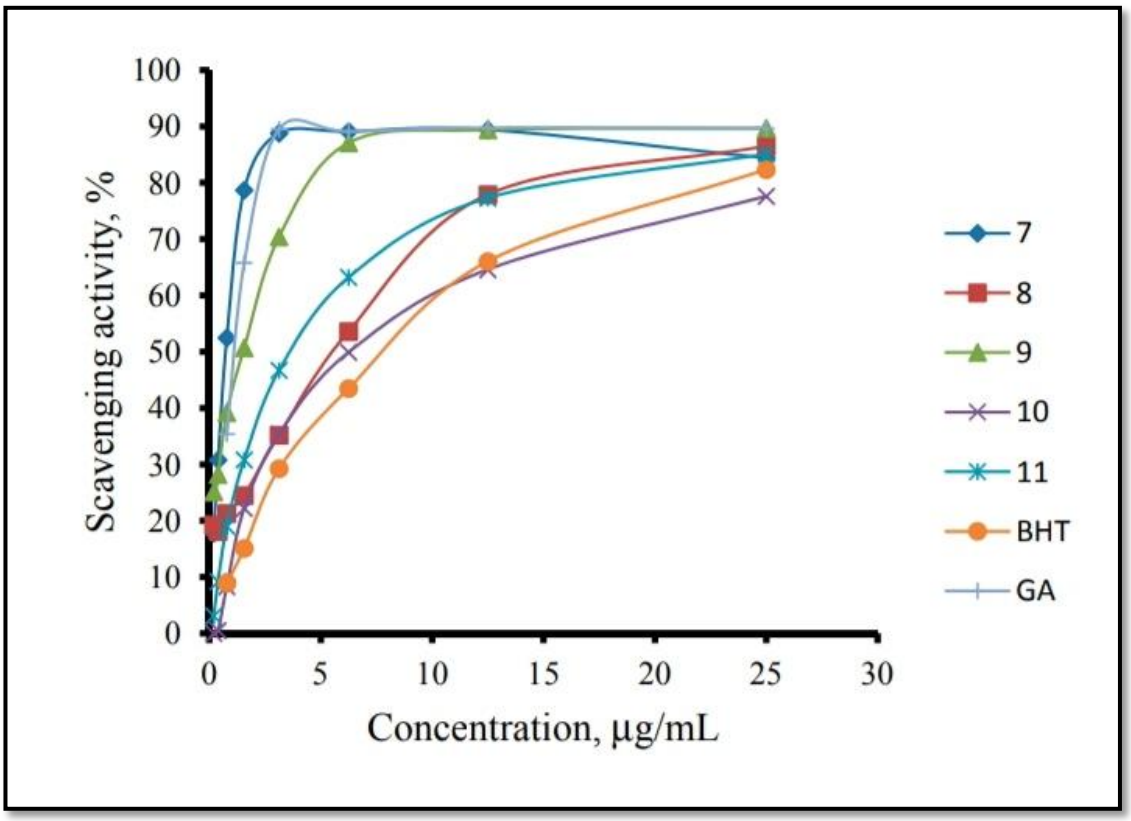

Figure 7 Scavenging activity of compounds 7–11 on DPPH radical.

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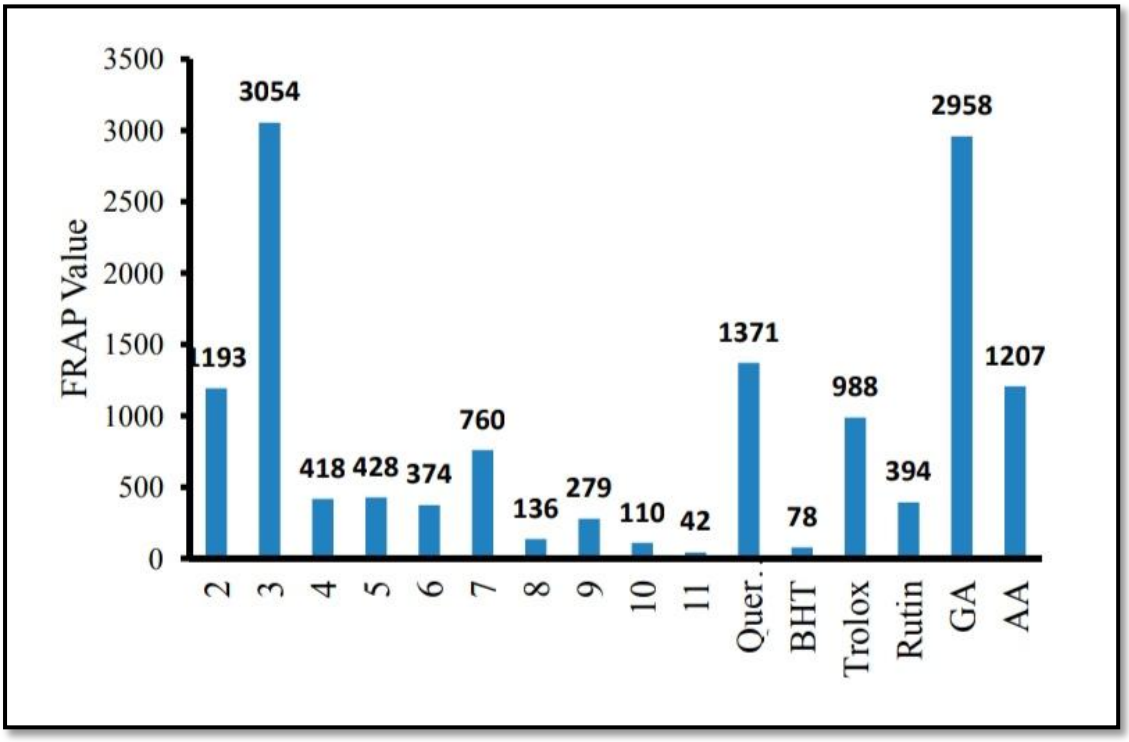
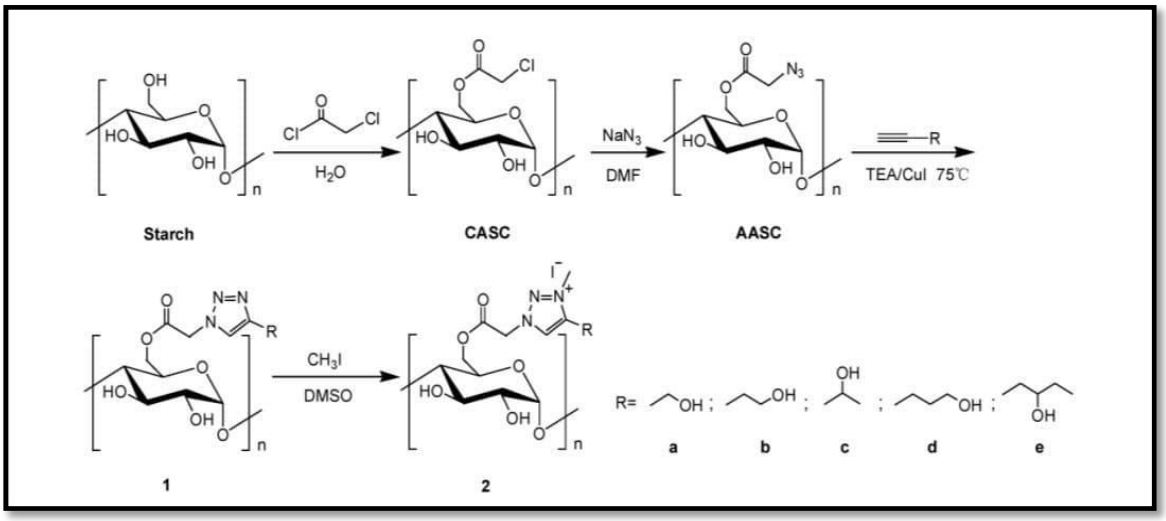


Figure 8.The ferric reducing antioxidant power (FRAP) Value for compound 2–11 and reference standard

Yuan Chen *etal* (47) Synthesis and antioxidant operation Using "click" reaction, five novel cationic 1,2,3-triazole functionalized starch derivatives,The radicals scavenging capacities of derivatives against hydroxyl radicals, DPPH radicals, and superoxide radicals were analyzed using FTIR and 1H NMR to test their antioxidant activity in vitro, Compared to pure starch, both starch derivatives have demonstrated marked antioxidant activity and are especially effective against superoxide radicals.



Scheme 16. Synthesis of the starch derivatives.

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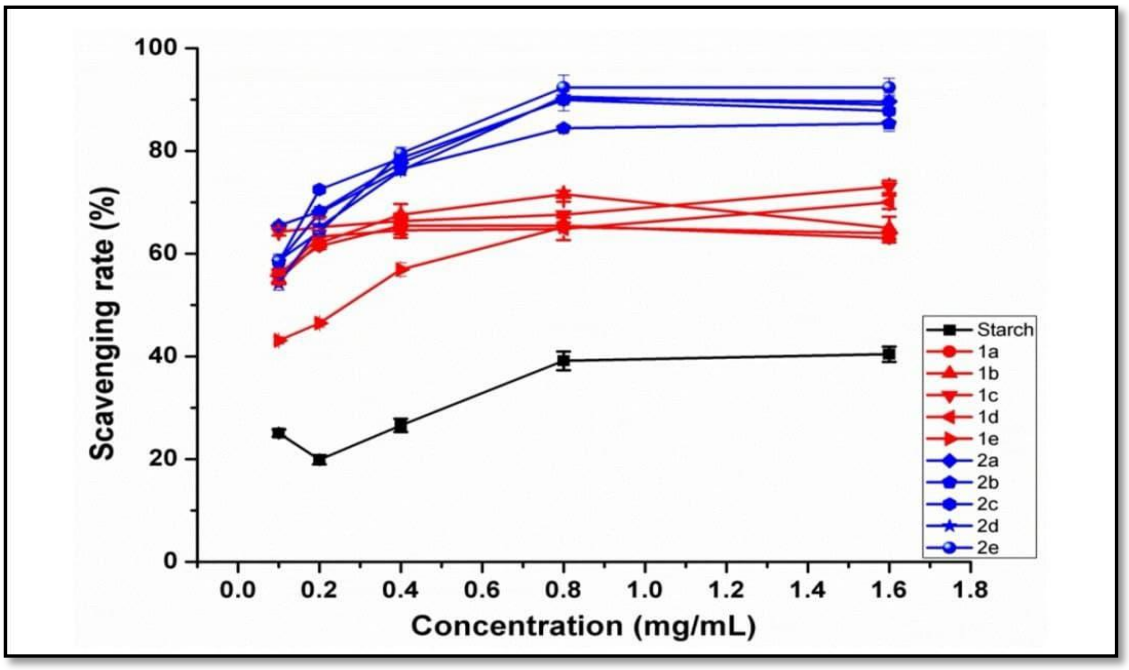

Figure 9. Hydroxyl radical scavenging activity of starch and starch derivatives.

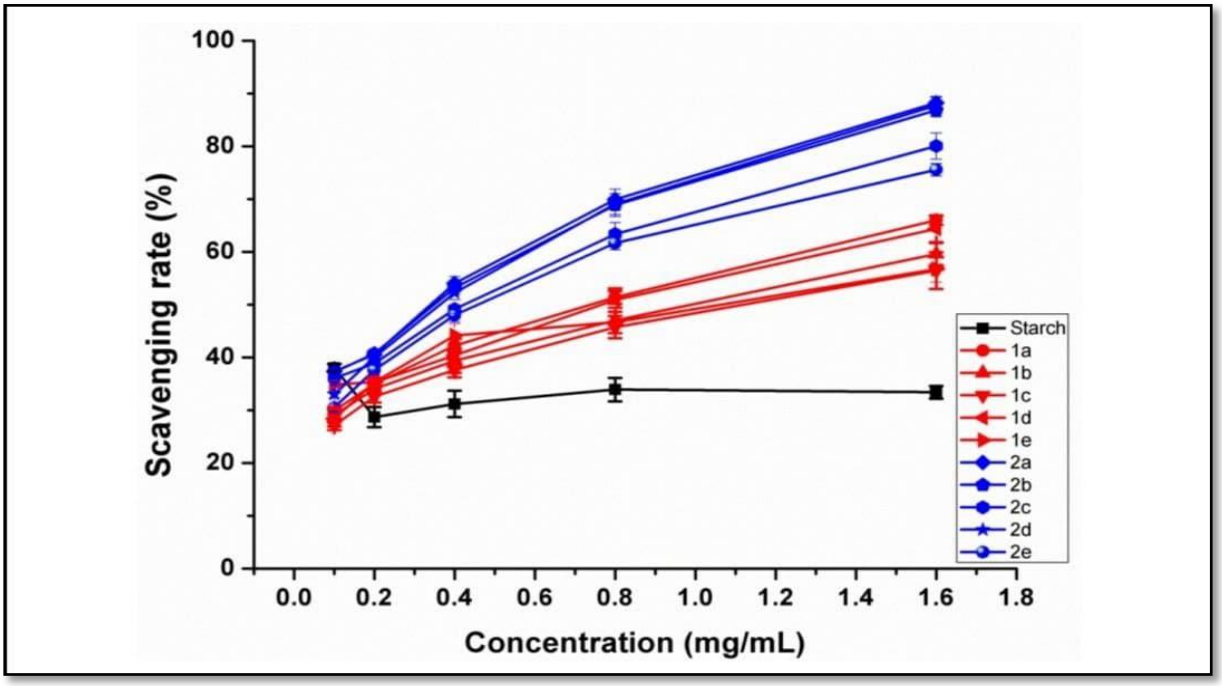

Figure 10. DPPH radical scavenging activity of starch and starch derivtive

Wagner O. Valença etal (48) Synthesis and antioxidant activity of nitroaryl-1,2,3-triazoles at moderate to good yields via 1,3-dipolar cycloaddition reaction (1,3- DCR) , by reaction nitroaryl-azide 1, terminal alkynes 2-16 together with stirring in presence CH3CN at room temperature under atmosphere of argon for 24 h ,

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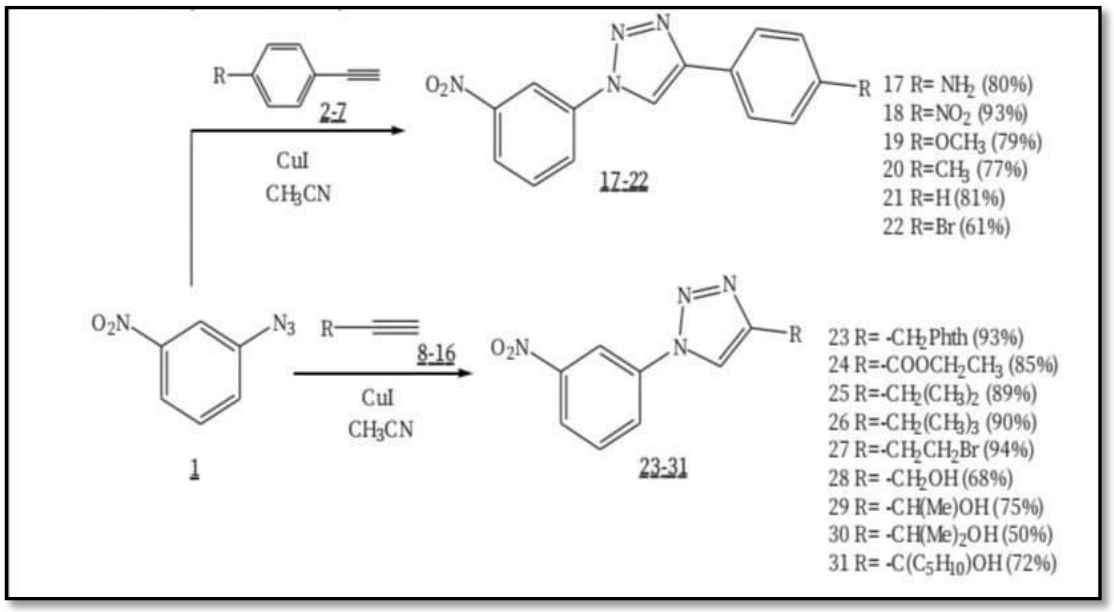
antioxidant activities are showed in three Compounds 17 (amine group), 28 and 29(hydroxyl group) more successful and can be used as antioxidant agent



Scheme.17 Synthesis of the nitroaryl-*1H*-1,2,3-triazole **17-31**

Table.7 The best results for antioxidant activities of nitroaryl-1H-1,2,3-triazoles

Compounds	EC_{50} (μg/mL) [a]	
	DPPH [b]	ABTS [b]
17	7.79 ±1.68	13.42 ±0.97
28	49.75 ±1.37	32.98 ±0.39
29	47.97 ±5.42	22.23 ±0.07
Ascorbic acid	1.67 ±0.02	-
TROLOX	-	3.86 ±0.04

Ali Shakir Razzaq etal (49) evaluation of antioxidant activities of new 1,2,3- triazole derivatives in vitro via pairing the single electron centered in nitrogen in DPPH with a hydrogen atom or by electronic donation, DPPH's deep purple color solution has intense absorption at 515-520 nm and turns yellow in the presence of an antioxidant that responds to 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radicals ,The potential of antioxidants to scavenge free radicals is the reduction of DPPH absorption at 517 nm, in add The combination of the 1,2,3-traizole ring with the 1,2,4-triazole ring together in the same matrix showed that the antioxidant strengthened

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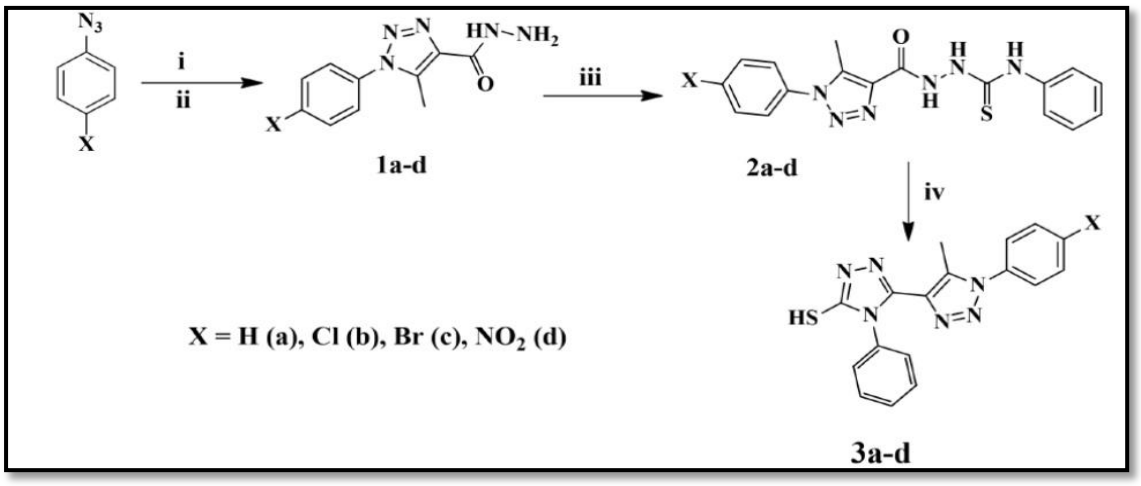

Scheme 18: i) Ethylacetoacetate, Et3N, DMF; ii) hydrazine hydrate, ethanol; iii) PhSCN, ethanol, reflux; iv) NaOH (2.0 N) reflux

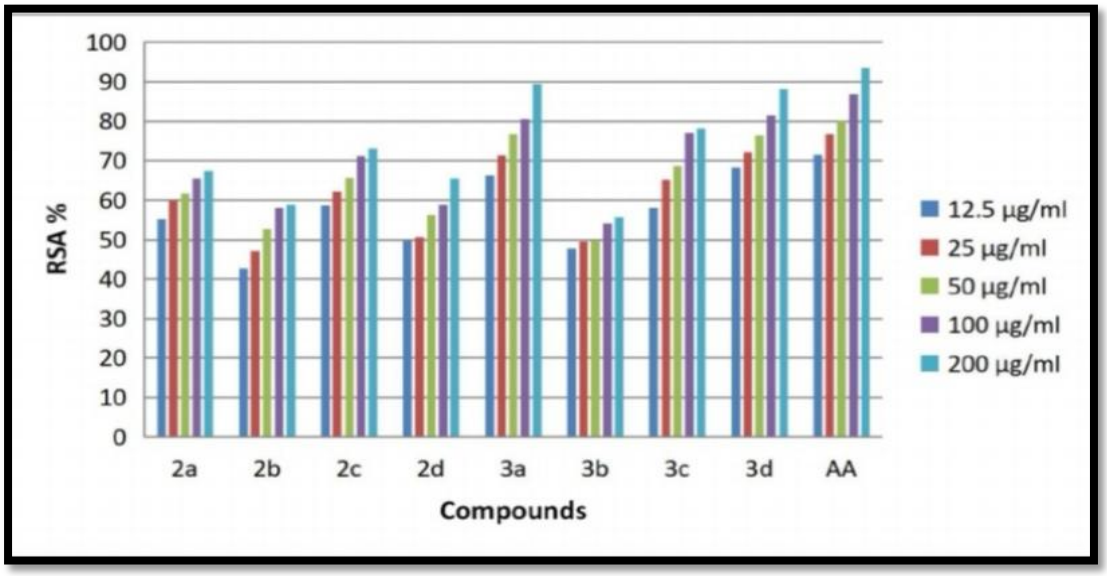

Figure 11: Antioxidant activity of DPPH scavenger radical for compounds 2a-d and 3a-d

Alisha Rani etal (50) 1,2,3-triazole-linked isosteres via CuAAC reaction by click chemistry Based on the number of the carbon atoms contained in the chain , which combines with Two moieties of 1,2,3-triazole . The 80a, 80b, and 80c compounds demonstrate excellent action against AChE, DPPH, and SOD . another class Compound 81 due to the presence of NO2 group and Molecule 82 due presence of diaryl sulfone moiety both have electron withdrawing groups, result strong behavior of antioxidants against DPPH comparison to A normal ascorbic acid due presence of electron donating group.the first , create complex and efficient drugs with high purity from simple and low cost starting materials

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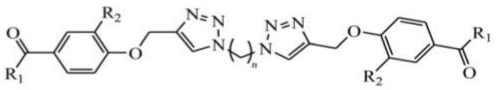
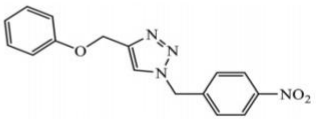
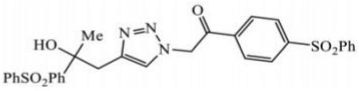
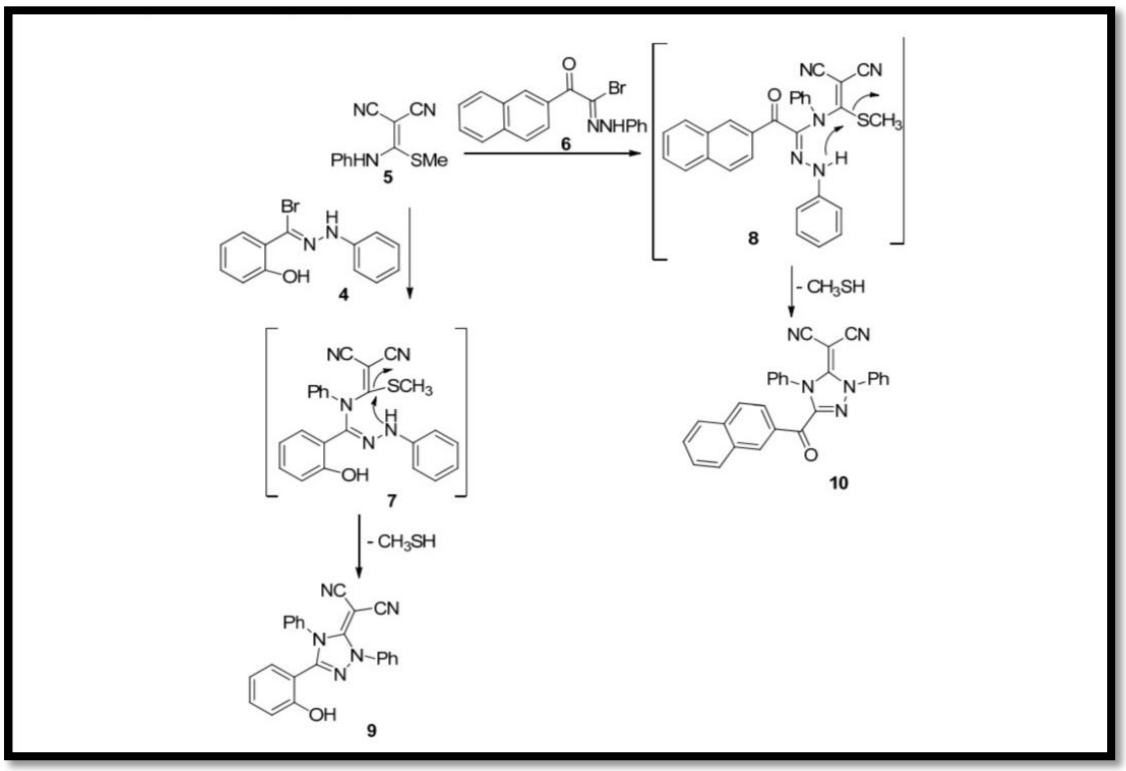
Sr. no.	Parent compound	Biological target	IC_{50} (μM)	Reference
80	 (a) R_1=CH_3 , R_2=H , n=10 (b) R_1=CH_3 , R_2=OCH_3 , n=4 (c) R_1=CH_3 , R_2=H , n=3	(a) AChE (b) DPPH (c) SOD	50.80 (±1.01) 113.63 (±0.05) 45.12 (±0.04)	124
81		DPPH	10.1	125
82		DPPH	20	126

Table 7 List of 1,2,3-triazole linked pharmacophore molecules possessing potent anti-oxidant activity

Mohammed A. Al-Omair etal (51) Synthesis of Novel Triazoles The use of readily available and reasonably accessible starting materials was accomplished by spectroscopic and elemental analyses, and tested via SOD-like action for their antioxidant activities, free radical scavenging activity of DPPH, ABST and NO. heterocycles triazoles were analyzed and tested for their biological properties, Excellent antioxidant activities were seen in compounds 5, 24 and 26h



Scheme 19. Synthesis of triazoline derivatives **9** and **10**.

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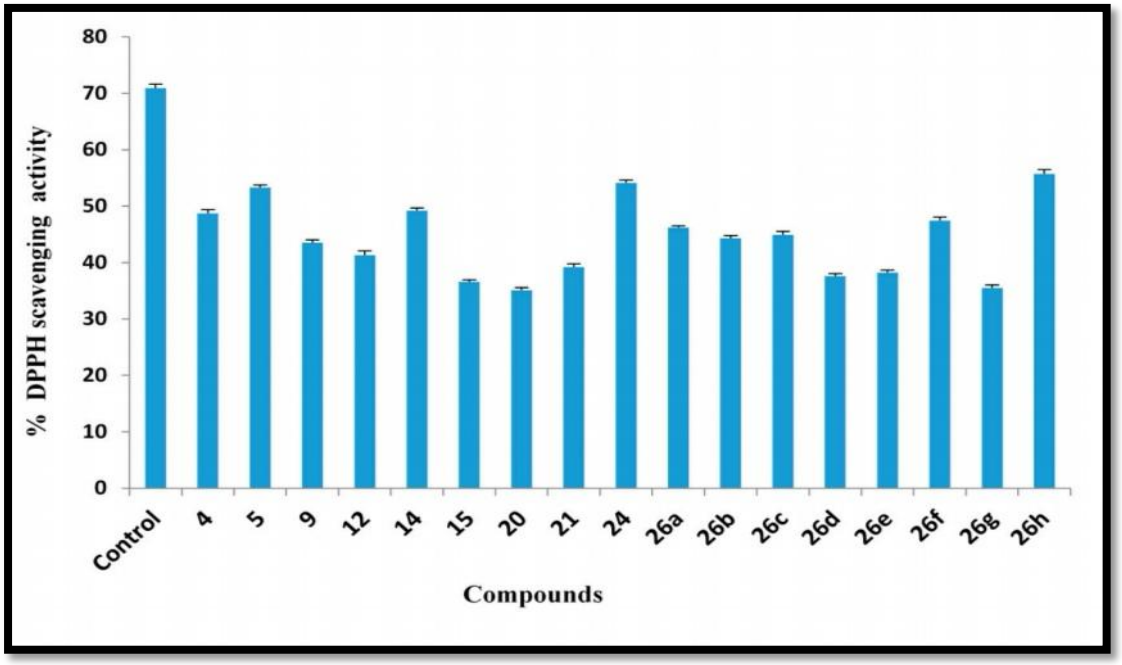

Figure 12. Antioxidant activities of compounds using DPPH

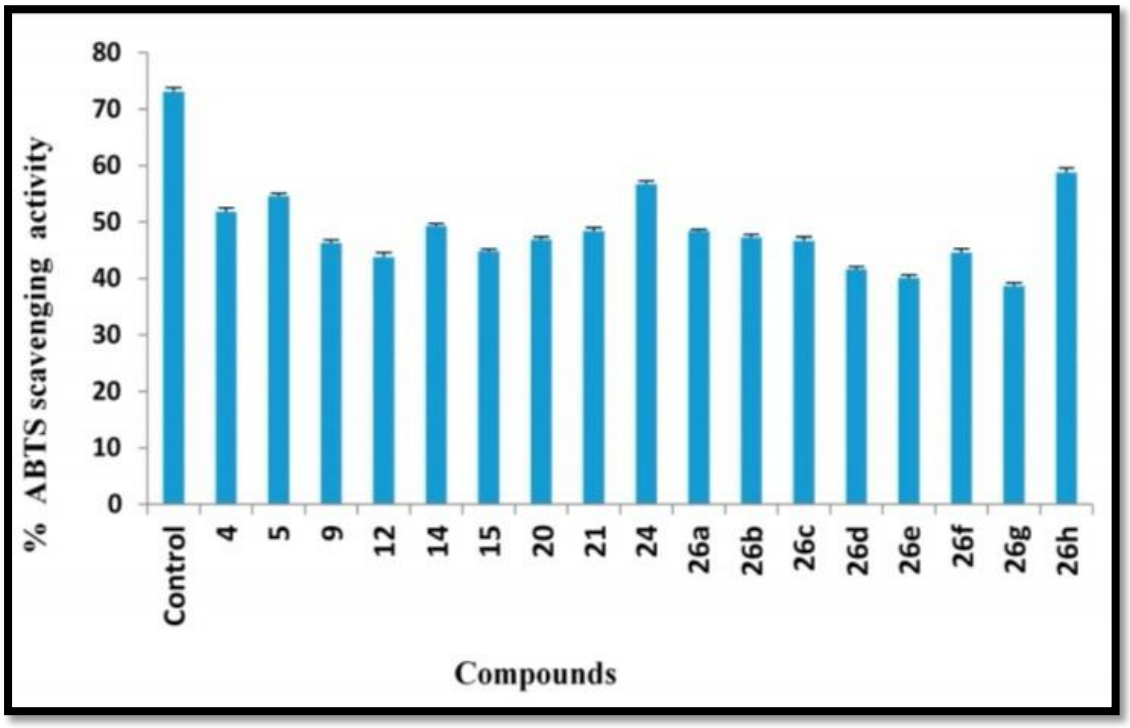

Figure 13. Antioxidant activities of compounds using ABTS.

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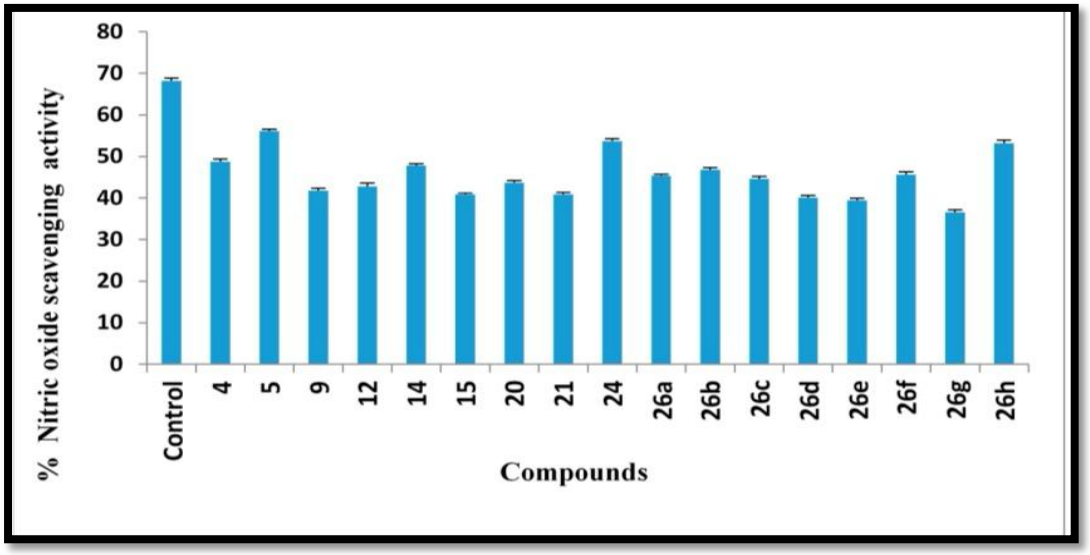
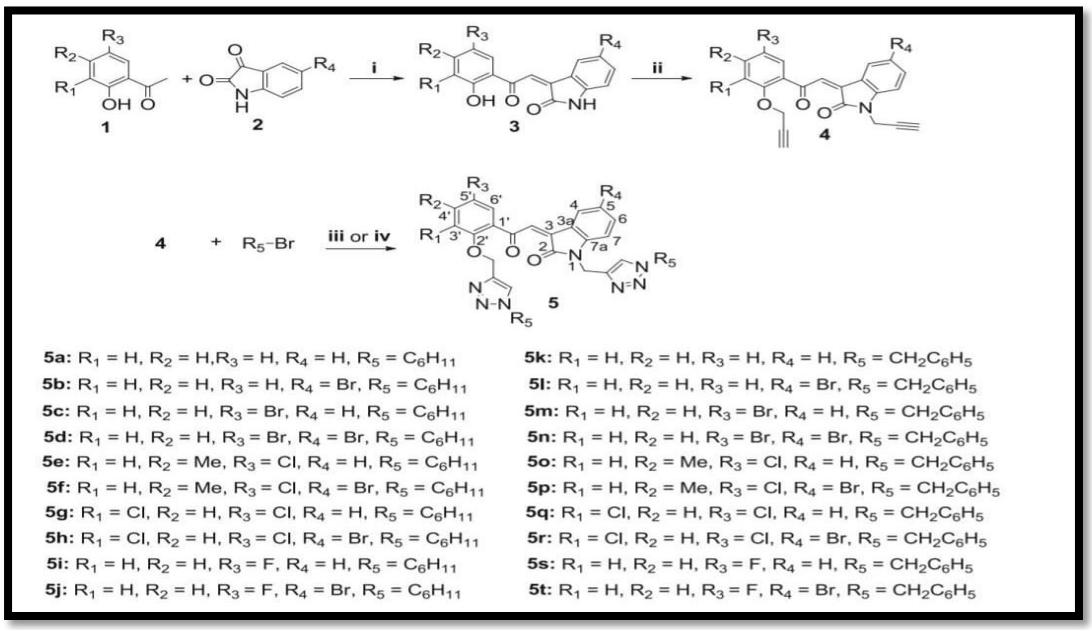


Figure 14. Antioxidant activities of compounds using NO.

Dongamanti Ashok etal (52) evaluation of 2-indolinone-based bis-1,2,3-triazole derivatives via Copper-catalyzed azide-alkyne 1,3-dipolar cycloaddition (CuAAC) of O-, N-propargylated indolinone derivatives , microwave-assisted reaction with organic azide produced in situ. According to electron donation capability or hydrogen atom Compounds 5(e , f) and 50 showed excellent radical scavenging activity among the compounds evaluated for antioxidant activity more than the normal ascorbic acid and BHT drugs .Bleaching of the purple-colored solution of methanol by 4 mL of 0.004 percent (w/v) DPPH methanol solution(reagent in spectrophotometric), 1 mL of different Methanol concentrations of the test compounds (5, 10, 25, 50 and 100µg/mL) were added, The absorbance was recorded against the blank at 517 nm after a 30-min incubation period at room temperature.



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Reagents and conditions: (i) KOH, EIOH, MWI, 100 W, 4-6 min; (i) propargyl bromide, K,CO,, dry acetone, reflux, 4-5 h; (i) NaN,, Cuso,.5H O, sodium ascorbate, t-BUOH/H,O (1:2), 80 °C, 12 h or MWI, 180 W, 10- 12 min; (iv) NaNa. Cul, DMF/H,O (1:2), 80 °C, 8 h or MWI, 180 W, 3-5 min;

Scheme 20. Rational drug design strategy of 2-indolinone-base bis-1,2,3-triazole

Table 8 Antioxidant activity in IC50 values and pharmacological parameters for the bioavailability of the synthesized compounds

Compounds	Scavenging activity (IC_{50} μM)			*c*log *P*[c]	Drug likeness[c]	Drug score[c]
	DPPH	NO	H_2O_2			
5a	22.75 ± 1.76	26.88 ± 1.51	24.72 ± 0.91	4.04	− 3.0	0.20
5b	22.89 ± 0.68	26.09 ± 0.96	28.47 ± 1.06	4.76	− 5.16	0.14
5c	27.71 ± 0.86	28.50 ± 0.40	19.79 ± 0.73	4.76	− 5.3	0.08
5d	34.91 ± 0.56	32.85 ± 0.71	36.84 ± 1.60	5.49	− 5.72	0.06
5e	15.71 ± 1.72	17.84 ± 0.73	14.85 ± 0.94	4.99	− 3.6	0.13
5f	17.46 ± 0.79	17.36 ± 1.97	17.82 ± 1.05	5.71	− 5.76	0.10
5g	28.75 ± 1.29	25.59 ± 0.75	31.04 ± 0.64	5.25	− 3.68	0.03
5h	44.43 ± 1.03	38.75 ± 0.39	51.72 ± 1.14	5.98	− 5.83	0.02
5i	30.12 ± 0.47	39.54 ± 0.72	31.60 ± 1.53	4.14	− 4.85	0.18
5j	30.66 ± 0.59	28.90 ± 0.83	26.97 ± 1.09	4.86	− 7.06	0.13
5k	22.73 ± 1.73	21.96 ± 1.45	22.07 ± 2.60	3.07	2.39	0.39
5l	20.84 ± 1.16	22.91 ± 1.00	23.70 ± 0.97	3.79	0.23	0.24
5m	24.93 ± 0.98	26.65 ± 1.53	22.99 ± 1.44	3.79	0.09	0.14
5n	33.05 ± 0.72	39.12 ± 0.82	39.93 ± 2.23	4.52	− 0.32	0.10
5o	15.02 ± 0.85	14.13 ± 0.80	16.82 ± 1.25	4.02	1.79	0.28
5p	26.04 ± 0.33	25.23 ± 1.01	20.54 ± 0.85	4.74	− 0.37	0.16
5q	24.60 ± 1.62	30.32 ± 1.07	24.25 ± 0.84	4.28	1.72	0.05
5r	46.56 ± 1.03	44.11 ± 0.75	43.78 ± 1.05	5.00	− 0.43	0.03
5s	29.18 ± 1.36	29.53 ± 1.99	34.32 ± 1.34	3.17	0.54	0.31
5t	22.47 ± 1.14	27.41 ± 1.23	28.03 ± 1.37	3.89	− 1.66	0.16
AA[a]	76.25 ± 3.92	94.48 ± 2.73	87.50 ± 5.90	− 2.46	0.02	0.74
BHT[b]	77.54 ± 1.14	88.27 ± 3.95	84.22 ± 1.78	4.82	− 9.12	0.04

Values are the means of three replicates ± SD
[a] Ascorbic acid
[b] Butylated Hydroxy Toluene
[c] Obtained from Osiris Property Explorer. Positive value of drug score indicates better suitability as drug

I. Vani*a* etal (53) Antioxidant Activity of Dimers containing chromene and triazole moieties combining biologically active heterocyclic rings into one molecular form, 1,2,3-triazole derivatives have been synthesized , are Caracterized by NMR, mass, and IR spectra of 1H and 13C .(DPPH), evaluated due donation capabilities of hydrogen atoms or electrons via Bleaching of the solution of purple methanol from 2,2-picrylhydrazyl-1-diphenyl-1 (DPPH) ,The absorbance after 30 min of incubation at room temperature Measured at 517 nm against blank.

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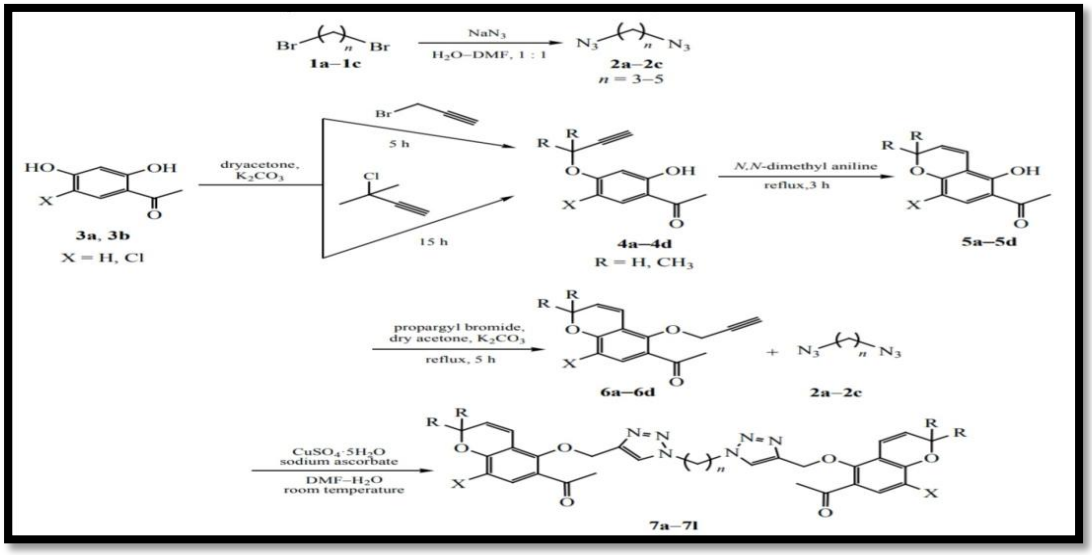

Scheme 21. Synthetic route to novel chromene based 1,2,3-triazole derivatives 7a–7l.

Table 9. Antioxidant activity of the synthesized compounds

Compound	Scavenging activity IC_{50}, µM	
	DPPH	H_2O_2
7a	21.75± 1.76	27.88±1.51
7b	23.89±0.68	28.09±0.96
7c	28.71±0.86	26.50±0.40
7d	35.91±0.56	33.85±0.71
7e	16.71±1.72	16.84±0.73
7f	16.46±0.79	19.36±1.97
7g	29.75±1.29	28.59±0.75
7h	43.43±1.03	36.75±0.39
7i	31.12±0.47	38.54±0.72
7j	32.66±0.59	29.90±0.83
7k	21.73±1.73	23.96±1.45
7l	21.84±1.16	21.91±1.00
Ascorbic acid	78.25±3.92	92.48±2.73

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Conclusion: -

In this review, we talked about an important topic, which is antioxidant activity, because it has a very important role in the human body by being able to slow down or prevent the oxidation of stray particles (free radicals) in vivo. Therefore, our need for antioxidants is inevitable and when free radicals exceed the available level of antioxidants, cells are threatened with the risk of oxidative stress, which would lead to cell death. The well-known antioxidants are vitamin C, vitamin E and selenium. Vitamin C is usually used as a compound. Standard with formulated compounds for being available, popular, inexpensive and important in nature, In this review, important compounds have been prepared, which are heterogeneous pentagonal rings, which are stable aromatics characterized by being of great biological effectiveness as anti-fungi, cancer and oxidative stress due to their containment of the nitrogen element with high electronegativity and the ability to give the electron, We noticed that the compounds containing one and two rings of triazole were effective very close to the standard vitamin C in most studies and with the various antioxidants used, One of the most important and well-known compounds used as standard antioxidants is DPPH,ABTS, trolox , gallic acid and linoleic acid. The DPPH (2,2-diphenyl-1-picryl-hydrazyl-hydrate) free radical process produces a violet solution in ethanol and is used as an antioxidant assay, In the presence of an antioxidant molecule, this free radical, which is stable at room temperature, is minimized, yielding a colorless ethanol solution, The IC50 value is a commonly used metric for determining the antioxidant function of research samples. It's measured as the antioxidant concentration used to reduce DPPH by 50%, As a consequence, the higher the antioxidant, the lower the IC50 value. We note in source 37 that compound d is the best compound as an anti-oxidant because it is less than IC50 and it is very close to the standard compound vitamin C as well in source 38 also compounds 4c, 4d They are the best compounds as they are closest to the standard ascorbic acid.

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