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Research article

Molecular modelling and evaluation on synthesised 2-phenyl-2,3-dihydro-4 h-chroman-4-one core against oxidative stress

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ABSTRACT

The aim of the study was to synthesis and characterization of 2,3-dihydro-4h-chroman-4-one core screened for antioxidant activity. The oxidative stress was related to the generation of Reactive oxygen species (ROS), which is responsible for the enhancement of several degenerative diseases, such as osteoarthritis, cancer, diabetes, cardiovascular diseases, *etc*. Due to this fact, the study was targeted for the development of myeloperoxidase inhibitor for overcoming the oxidative stress. The molecular docking analysis were afforded that the titled compounds possess noteworthy potency against myeloperoxidase (PDB ID: 1DNU). The docking simulation of seven hybrid of flavanone showed the better binding score ranging between -6.66 to -8.56 kcal/mol. Based on the result, the synthesised compounds were screened for the evaluation of various *in-vitro* antioxidant studies by hydroxy radical and nitric oxide radical scavenging assay. In which, the hydroxyl substituted flavanones (HFA3-HFA7) were afforded significant IC_{50} values compared with their respective standards due to their electron donating property which foraging the radicals responsible for oxidative stress were noted. Among the synthesised compounds, HFA5 and HFA6 produced excellent free radical scavenging on hydroxyl radical and nitric oxide radical methods were observed. From which the study initiated that synthesised flavanone core with hydroxyl and electron donating groups over the moiety should helpful in the management of major chronic diseases were initiated.

Keywords: Antioxidant, Flavanone, Reactive oxygen species, Myeloperoxidase, Chronic ailments.

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INTRODUCTION

Flavonoids are a class of bioactive chemicals present in a wide range of plant-based diets. Regular intake has been linked to a lower risk of a variety of chronic diseases, including cancer, cardiovascular disease (CVD) and other degenerative disorder. Flavonoids are divided into subgroups based on their chemical structure such as Flavones, flavanones, flavonols, flavan-3-ol, isoflavones and anthocyaninsetc[1]. At the molecular level, they have antioxidant properties as well as the potential to influence a number of critical enzymatic pathways. Flavonoids appear to serve a helpful function in illness prevention, according to a growing body of scientific research, but further clinical and epidemiological trials are under progress for further need. Flavanoids are rich in vegetables, fruits, nuts and seeds, consumption of those in our daily diet should be beneficial for our healthy biological system.

One of the flavonoid analogues, flavanone was selected as a titled compound those are aromaticketones in nature which are derived from plant glycosides [2,3]. Particularly the enzyme chalcone isomerase is necessary to produce flavanone in plants. Based on this aspect, the present study deals on chalcone analogues those were prepared synthetically by Claisen condensation reaction and cyclised further to produce flavanone were designed. Flavanones (2-phenyl-chroman-4-one) are heterocycles comprised three phenyl rings in which two phenyl rings were connected with pyran ring and compound is not bearing double bond (no unsaturation). Flavanones are polyphenolic in nature those are existed in plants as naringenin, hesperidin, heridictyol and isosakuratenin [4].

Scientific research urged the emergence of the prevention of chronic diseases like cancer, diabetes, neurodegenerative disorders, and on. According to population studies, some of the chronic diseases like cardiovascular disorder (80 %), type 2 diabetes (90 %), and cancer (30 %) could be ducked by their lifestyle and diet changes. The recent literature strongly depicts that oxidative stress should be a primary or indirect cause of chronic diseases sometimes

which due to their aging factors. Subsequently, a great deal of scientific attention and resources has been spent on the significance of antioxidants in preventing oxidation and, as a result, avoiding or delaying oxidative stress. By which oxidative process and its pathways on different enzymes are accountable for the development of chronic diseases. In which, an exogenous and endogenous antioxidant also plays a role in overcoming those ailments [5].

Oxidative stress should influence directly or indirectly by intracellular signal transduction, gene mutation and transcription factors result in cellular damage. These are a key principle for many chronic diseases including carcinogenesis and other degenerative illnesses [6]. In tissues, reactive oxygen species can harm DNA, proteins, carbohydrates, and lipids. A system of enzymatic and nonenzymatic antioxidants that remove prooxidants and scavenge free radicals regulates these potentially harmful processes [7]. Antioxidants in healthy people should helpful in overcoming the dangerous ailments even carcinogen on the other hand elevation of ROS should worsen the disease in another extension [8,9].

Based on this aspect, importance of antioxidant property must give a therapeutic efficacy in chronic ailments were clearly depicted. Hence the present study deals with synthesis of naturally representing flavonoid analogue especially flavanone core from cyclisation of chalcone derivatives. The synthesised compounds were characterised by various spectral techniques and evaluated for antioxidant property by various *in vitro* methods. The molecular docking study was subjected for prediction of the binding score and binding interactions of synthesized core were observed.

MATERIAL AND METHOD

Materials

Sigma Aldrich, Himedia Pvt.ltd, Nice chemicals, Merck, and SD fine chemicals provided all of the chemicals, solvents, and reagents used in this investigation. The melting points were calculated using open glass capillary tubes. Merck silica gel-G TLC plates were used to assess reaction progress and purity using thin layer chromatography. The TLC spots were observed using an iodine chamber or a UV lamp. Using a Shimadzu Ultra visible spectrophotometer measured the maximum absorbance (λ_{max}). KBr pellets technique were used to determine the compound's IR spectra on an FT-IR Shimadzu. The elemental analysis (CHNSO Analyzer), mass spectrometry (HRMS mass spectrometer), ^{1}HNMR andC^{13} NMR spectroscopy by FT-NMR (500 & 100 MHz respectively) were recorded at the Indian Institute of Technology in Chennai.

Software required

Molecular graphics laboratory (MGL) tools and Auto Dock 4.2 were obtained from www.scripps.edu, Chem Sketch from www.acdlabs.com, and Discovery studio visualizer 2.5.5 from www.accelrys.com. Openbable.org was used to convert the Mol file of Ligand to the PDB format.

Preparation of enzymes and ligands

The enzyme selected for this study Myeloperoxidase (PDB: 1DNU), X-ray crystal structures were downloaded from protein data bank rcsb.pdb.orgportal[10]. The enzyme should be refined and purified by deletion of water; heteroatoms and addition of kollmann charges were accomplished. The ligand was optimised by minimizing their energy, added with gasteiger charges and polarhydrogensaswell torsion was set.

Molecular Simulation

The refined proteins and ligands (HFA1-HFA7) (energy minimized) were assessed for molecular simulation for predicting their binding affinity and key residual sites over the enzyme [11,12]. In that grid map should be fixed with 90 points, Lamarckian genetic algorithm was accomplished with 25,000,000 energy evaluations, for each run 5,000 generations were done and 150 docking runs were achieved.

Synthesis of Flavanones

The chalcone derivatives [13-14] were produced according to the reported technique, followed by the production of new flavanones. The (0.108 mole) substituted chalcone dissolved in (6 mL) methanol and (1 mL) 10% hydrochloric acid were added. After 1.5 hours of refluxing, (2.15 mole) sodium acetate was added to the reaction mixture [15]. Further continue the reflux for 3 hours, then cooled and mixed with (25 ml) water and extract with (30 ml) two proportions of ethyl acetate. After extraction, organic layer was separated and dried over magnesium sulphate to achieve required flavanone derivatives (HFA1-HFA7) mentioned in scheme.1. Recrystallized the compounds with aqueous methanol

Scheme 1. Synthesis of titled compounds

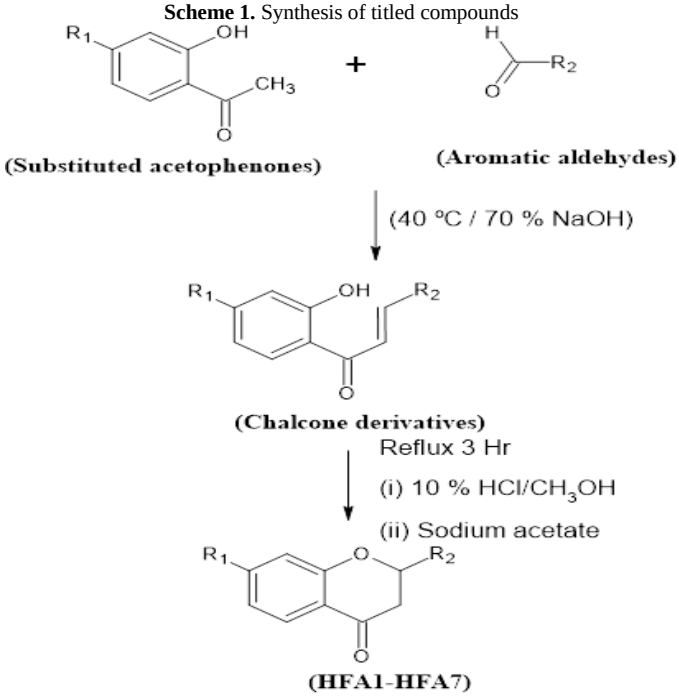


Table 1:Substitution Pattern of titled compounds

Code	R_1	R_2
HFA1	-OH	$-C_6H_4$-2(OH)
HFA2	-OH	$-C_6H_4$-2(Cl)
HFA3	-OH	$-C_6H_4$-4(Cl)
HFA4	-OH	$-C_6H_4$-4(OCH_3)
HFA5	-OH	$-C_6H_3$-3(OCH_3)- 4(OH)
HFA6	-OH	$-C_4H_3S$
HFA7	-OH	$-C_4H_3O$

***In-vitro* evaluation of antioxidant activity**

Hydroxyl Radical Scavenging Method

The (1 ml) of synthesised compounds (HFA1-HFA7) and the standard drug (gallic acid) at various concentrations as 10, 20, 40, 80, and 160 µg/ml were added to (1 ml) Iron-EDTA solution, (0.5 ml) 0.018 % EDTA, (1 ml) DMSO and (0.5 ml) ascorbic acid as per the reported literature[16-17]. The reaction mixtures were firmly sealed and heated for 15 minutes at 80 to 90 ̊C. To inhibit the reaction, add (1 ml) cold trichloroacetic acid, after heating add(3 ml) Nash reagent (75 gm ammonium acetate, 2 ml acetyl acetone, and 3 ml glacial acetic acid) stirred thoroughly and make over the volume up to 1 L using distilled water. Keep aside for incubation (15 minute) for the sake of colour development. The colour was measured at 412 nm with blank solution (without sample in reaction mixture).

Nitric oxide scavenging assay method

The (1 ml) synthesised compounds (HFA1-HFA7) and reference compound (gallic acid) were mixed with (0.5 ml) sodium nitro prusside (5mM in phosphate buffered saline pH 7.4) and incubated at 25ºC for 180 minutes[18-19]. The reaction mixture was mixed with an equal amount of Griess reagent leads to colour formation due to diazotisation of nitrite ions, because of sulphanilamide (1 %) and naphthyl ethylene diamine dihydrochloride (0.1 %) in phosphoric acid (5 %) existed in griess reagent. The chromophore was observed at 540 nm against blank solution (without sample). The methods were repeated thrice and mean should be calculated for determination of percentage inhibition by following formula.

$$\% \text{ Inhibition} = A_c - A_t / A_c \times 100$$

Where A_t = Absorbance of Test, A_c = Absorbance of Control

STATISTICAL ANALYSIS

The results of pharmacological investigations are reported as mean ± standard error of the mean (SEM). The significance of differences between the control and tested groups was determined using an ANOVA (Dunnett's t- test) with P value lesser than 0.05 were considered as significant.

RESULT AND DISCUSSION

The chalcones were produced and cyclized to form lead flavanones according to the methodology (HFA1-HFA7). Spectroscopic techniques such as UV, IR, H^1NMR, C^{13}NMR, and GCMS were used to characterise the synthesised candidates. The maximum absorbance of the title compounds in UV spectroscopy ranged from 284 to 367 nm[20]. The explanation for this is the presence of, unsaturated carbonyl groups in the title compounds, which causes $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions.

The C-Cl stretching of flavanones (HFA2 & HFA3) yielded absorbance in the range of 609–680 cm^{-1} in IR spectroscopy. The compound HFA4, Ar-OCH_3 stretching is confirmed by an IR absorption peak at 2948–2999 cm^{-1}. Retro Diels Alder fission was used to play a role in the mass fragmentation pattern of hybridised flavanones[21]. The relevant parent ion peaks of the synthesised flavanones correspond to the predicted molecular weight were noted. The presence of two protons on ring C is confirmed by H^1-NMR peaks at 5.6–7.2 ppm. Similarly, titled compounds were confirmed with their hydroxyl substitution on ring A were observed at 8.7–9.3 ppm in H^1NMR. Methoxy (HFA4) group also generated their respective peakin shielding field which denoted its substitution over the flavanone core. The physical data of the synthesised compounds were mentioned in the table.2. and spectral data of those compounds and proposed scheme were reported previously in our last publication[15].

Docking Study

For the evaluation of antioxidant property, molecular simulations of synthesised flavanones (HFA1-HFA7) were displayed in table.3. The docking score of the synthesised compounds has considerable interactions with the enzyme compared with reference drug ascorbic acid.

Myeloperoxidase (MPO) is a member of the peroxidase family that is usually found in case of inflammation during protein oxidation, particularly in cardiovascular diseases, renal diseases, and brain ailments[22]. During the respiratory burst of neutrophils, this enzyme catalyses the synthesis of hypochlorous acid from hydrogen peroxide. In the presence of hydrogen peroxide, this also converts tyrosine to tyrosine radical. Oxidative stress in the tissues was caused by the presence of hypochlorous acid and the tyrosine radical[23-25]. Because of this, this enzyme was chosen as a suitable target for assessing antioxidant properties.

Among the synthesised compounds HFA5 and HFA6 were possess significant dock score(-8.93 & -8.51 respectively) compared with the standard were showed in the Table.2. The compound 2e and 2f produced hydrogen bond interactions (Ala 31, 35, Arg 323 and Ile 360respectively) and for hydrophobic interactions (Arg 31 and Ala 35 respectively) were showed in the Fig. 2.

Based on the docking result of synthesised compounds on myeloperoxidase were revealed the antioxidant property of the compounds. Due to this aspect, those compounds were possessing the free radical scavenging role by which the management of diabetic mellitus and also favourable for overcoming the diabetic complications due to oxidative stress.

The antioxidant property of the compounds was disclosed

based on the docking results of synthesised compounds on myeloperoxidase. On this aspect, synthetic flavones have free radical scavenging role as like that of naturally available flavonoids, could helpful in the management of many major diseases like diabetic mellitus, cancer and neuro degeneration disorders, those were worsened due to oxidative stress on long term therapeutic regimen.

Table 2: The physical data of synthesised flavanones

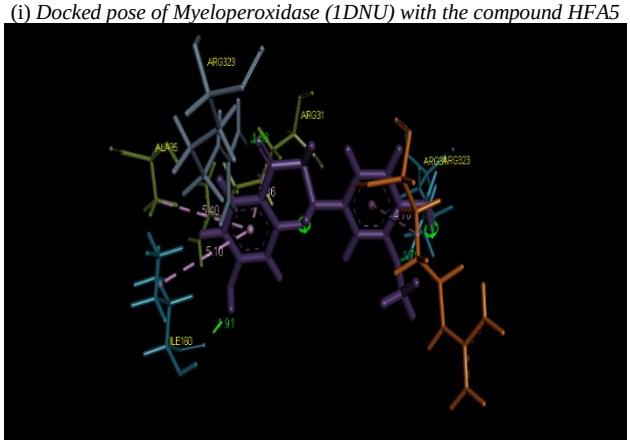
CD	Mol.Form & Mol.wt	Description	Solubility	R_f value	Elemental analysis		MP (°C)	% yield
					Calculated	Find		
HFA1	$C_{15}H_{12}O_4$, 256	Brownish powder	Ethyl acetate, DMSO, DMF, methanol &ethanol	0.82	C [70.31 %] H [4.72%] O [24.97 %]	C [69.96 %] H [5.33 %] O [24.84 %]	229-232	32.5
HFA2	$C_{15}H_{11}ClO_3$, 274	Reddish brown powder	Ethyl acetate, DMSO & DMF	0.90	C [65.58 %] H [4.04%] Cl [12.91 %] O [17.47 %]	C[65.49 %] H [4.86 %] Cl [12.81 %] O [17.32 %]	195-198	50.8
HFA3	$C_{15}H_{11}ClO_3$, 274	Brown color powder	Ethyl acetate, DMSO, DMF, methanol & ethanol	0.74	C [65.58%] H [4.04%] Cl [12.91 %] O[17.47 %]	C [65.43 %] H [4.63 %] Cl [12.86 %] O [17.15 %]	210-214	72
HFA4	$C_{16}H_{14}O_4$, 270	Pale yellow powder	Ethyl acetate, DMSO, DMF & methanol	0.70	C[71.10%] H[5.22%] O[23.68 %]	C[69.91 %] H[5.92 %] O[23.44 %]	232-235	69.2
HFA5	$C_{16}H_{14}O_5$, 286	Brown color powder	Ethyl acetate, DMSO, DMF & Chloroform	0.86	C[67.13 %] H[4.93%] O [27.94 %]	C[66.93 %] H[5.21 %] O[27.57 %]	276-279	63.4
HFA6	$C_{13}H_{10}SO_3$, 246	Brown color powder	Ethyl acetate, DMSO, DMF & methanol	0.54	C[63.40 %] H[4.09%] O[19.49 %] S[13.02%]	C[63.14 %] H[4.73 %] O[19.09 %] S[12.95 %]	166-169	73.4
HFA7	$C_{13}H_{10}O_4$, 230	Pale yellow powder	Chloroform, ethyl acetate, methanol, DMF and DMSO	0.67	C[67.82 %] H[4.38%] O[27.80 %]	C[67.74 %] H[4.28 %] O[27.59 %]	181-185	65.4

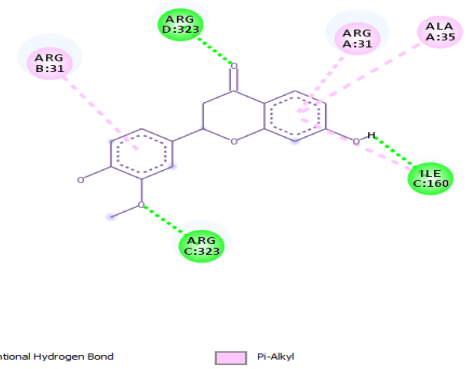
Table 3: Docking score of synthesised flavanones on Myeloperoxidase

Compound code	Docking score ΔG (Kcal/mole)
HFA1	-8.09
HFA2	-7.88
HFA3	-7.92
HFA4	-8.35
HFA5	-8.93
HFA6	-8.51
HFA7	-8.01
Ascorbic acid	-8.66

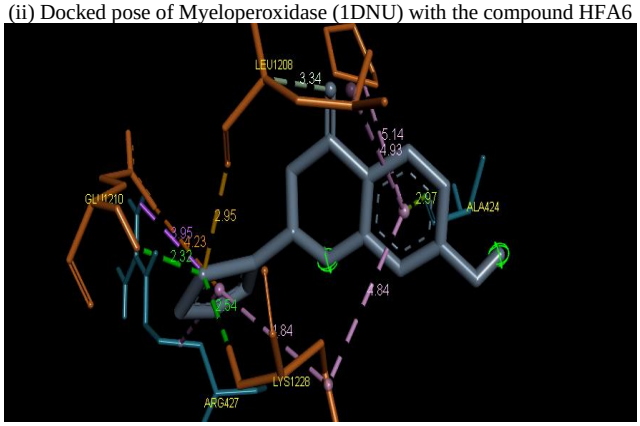
Figure 2: Visualization of synthesized ligand (flavanones) interaction with Myeloperoxidase

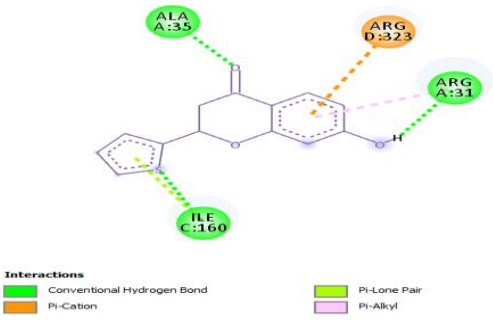
(i) *Docked pose of Myeloperoxidase (1DNU) with the compound HFA5*





(ii) Docked pose of Myeloperoxidase (1DNU) with the compound HFA6





In-vitro evaluation of antioxidant activity

Hydroxyl Radical Scavenging Method

In Table.3 were mentioned the percentage inhibition of hydroxyl radical scavenging for synthesised flavanones.

When the percentage inhibition was compared to the standard gallic acid, the synthesised flavanones (HFA3-HFA7) produced the highest percentage inhibition on the hydroxyl radical. When compared to the reference, the IC_{50} values of those synthesised compounds (HFA3-HFA7) were significant (66.3, 51.1, 46.9, 53.9, and 48.8 µg/ml, respectively) and for standard 39.6 µg/ml (Diclofenac sodium) were observed.

All values are Mean ± SEM, n = 3. One way Analysis of Variance (ANOVA) followed by Dunnett's test was performed as the test of significance.

Nitric Oxide Scavenging Activity

In general, nitric oxide radicals are produced in human bodies by the amino acid (L – arginine) found in endothelial cells and phagocytes. Being an unpaired electron free radical that interacts with superoxide anion to create peroxy nitrite (ONOO.) These radicals were very toxic, causing inflammation as a result of cellular damage, which resulted in juvenile diabetes, scelorosis, ulcerative colitis, arthritis, and other condition. As a result, the current research focuses on the *in-vitro* scavenging of nitric oxide by synthesised molecules at various doses.

The sodium nitro prusside is used as a source of nitric oxide in this approach, which interacts with oxygen to produce nitrite ions. The Griess reagent comprises sulphanilamide, which is diazotized with nitrite ions to generate diazonium salt, which then combines with naphthyl ethylene diamine leads to complex formation (pink colour). The decrease in optical density of the pink colour complex was directly related to nitric oxide scavenging. The scavenging activity of titled compounds leads to compete oxygen interaction and retard nitrite radical formation which reflected in pink color formation with griess reagent were noted. Hence drug concentration is inversely proportional to color formation (absorbance).

Table. 3. Antioxidant Effect of synthesised Flavones by Hydroxyl Radical Scavenging Assay (HRSA)

Compounds	Percentage Inhibition of HRSA					
	10 µg/ml	20 µg/ml	40 µg/ml	80 µg/ml	160 µg/ml	IC_{50}
HFA1	19.6±1.45	32.54±1.76	45.69±2.57	59.8±2.48	79.52±2.72	69
HFA2	20.34±1.55	34.9±2.06	47.83±2.36	65.31±2.61	81.46±2.86	62.1
HFA3	19.38±1.59	31.49±1.69	46.58±1.69	63.76±2.86	80.59±2.94	66.3
HFA4	21.76±1.55	35.58±1.53	53.42±1.96	71.32±2.75	91.83±2.90	51.1
HFA5	22.53±1.60	37.75±1.68	54.59±2.43	74.39±2.66	94.73±2.77	46.9
HFA6	19.83±1.53	34.64±1.73	51.58±2.61	71.43±2.29	90.39±3.32	53.9
HFA7	20.37±1.58	38.29±1.83	54.73±2.34	74.69±2.35	89.75±2.98	48.8
Gallic acid	23.96±1.63	42.27±2.18	58.69±1.54	77.21±1.72	98.57±1.67	39.6

Table.4. Antioxidant Effect of Synthesised Flavanones by Nitric Oxide Scavenging Assay

Compounds	% Inhibition of Nitric Oxide Scavenging					
	10 µg/ml	20 µg/ml	40 µg/ml	80 µg/ml	160 µg/ml	IC_{50}
HFA1	20.9±1.37	35.26±1.29	49.2±2.10	63.71±2.72	79.37±3.09	62.9
HFA2	21.4±1.17	34.62±1.58	48.51±1.86	64.7±2.99	81.9±3.05	61.4
HFA3	20.18±1.35	36.4±1.49	47.91±2.07	62.7±2.81	76.95±2.94	65.5
HFA4	20.36±0.96	35.8±1.35	49.6±2.18	66.8±1.84	80.63±2.65	60.3
HFA5	23.5±1.21	38.4±1.66	52.7±2.31	67.12±1.95	84.6±2.47	53.3
HFA6	22.7±0.98	35.81±1.57	47.85±2.19	61.47±2.31	78.6±2.95	64.2
HFA7	19.56±1.47	33.6±1.67	47.81±1.96	65.12±2.43	78.67±2.82	64.9
Gallic acid	32.27±1.93	45.25±2.46	62.34±1.74	80.22±2.56	98.1±2.88	28.8

CONCLUSION

As like that of naturally available flavonoids, synthesised flavanones were produced their antioxidant property were determined and observed. The hybridised flavanones (HFA1-HFA7) were synthesised from cyclisation of chalcone analogues and characterised by various spectroscopic techniques as UV, FT-IR, H^1NMR, C^{13}NMR and GCMS. Those synthesised compounds were screened for antioxidant activity by molecular docking study on the target myeloperoxidase enzyme. Further those compounds were tested for various *invitro* evaluation like hydroxyl radical scavenging and nitric oxide scavenging activity. In both methods, the IC_{50} values were calculated and afforded noteworthy result on scavenging these radicals were observed also well correlated with docking result. The present study concluded that hypothesis of this research was satisfied, which paves the futuristic way in drug discovery by which development and further screening on particular chronic diseases should produce therapeutic efficacy along with antioxidant property.

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REFERENCE

1. Erica L S, Beatriz H L N, Sales M, Aurea P F, Sirlei D T, 2017. Flavonoids Classification, Biosynthesis and Chemical Ecology, Flavonoids From Biosynthesis to Human Health, Goncalo C. Justino, Intech Open, 54574
2. National Center for Biotechnology Information, 2021. PubChem Compound Summary for CID10251, Flavanone *PubChem*. Accessed 27.
3. Das A B, Goud V, Das C, 2019. Phenolic compounds as functional ingredients in beverages. InValue-Added Ingredients and Enrichments of Beverages. Academic Press, 1 pp. 285-323.
4. Willcox J K, Ash S L, Catignani G L, 2004. Antioxidants and prevention of chronic disease. Critical reviews in food science and nutrition. 1; 44 (4):275-95.
5. Ayar A, Aksahin M, Mesci S, Yazgan B, Gül M, Yıldırım T, 2021. Antioxidant, cytotoxic activity and pharmacokinetic studies by SwissAdme, Molinspiration, Osiris and DFT of PhTAD-substituted dihydropyrrole derivatives. Current Computer-aided Drug Design. 22.
6. Di Mascio P, Murphy M E, Sies H, 1991. Antioxidant defense

systems the role of carotenoids, tocopherols, and thiols. The American journal of clinical nutrition. 1;53(1):194S-200S.

7. Harris I S, De Nicola G M, 2020. The complex interplay between antioxidants and ROS in cancer. Trends in cell biology. 1;30 (6):440-51.
8. Blair-Johnson M, Fiedler T, Fenna R, 2001. Human myeloperoxidase: structure of a cyanide complex and its interaction with bromide and thiocyanate substrates at 1.9 A resolution. Biochemistry. 20;40(46):13990-7.
9. Kiruthiga N, Prabha T, Selvinthanuja C, Srinivasan K, Sivakumar T, 2018. Multidocking Studies on 2-Phenyl-4h-Chromen-4-One Hybrid and Evaluation of Anti-Diabetic Activity. Journal of Pharmaceutical Sciences and Research. 1;10(12):3018.
10. Kiruthiga N, Alagumuthu M, Selvinthanuja C, Srinivasan K., Sivakumar T, 2021. Molecular modelling, synthesis and evaluation of flavone and flavanone scaffolds as anti-inflammatory agents. Anti-Inflammatory & Anti-Allergy Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Inflammatory and Anti-Allergy Agents). 1;20(1):20-38.
11. Kiruthiga N, Saravanan G, Selvinthanuja C, Srinivasan K, Sivakumar T, 2021. Glycolytic Inhibition and Antidiabetic Activity on Synthesized Flavanone Scaffolds with Computer Aided Drug Designing Tools. Letters in Drug Design & Discovery. 1;18 (6):574-92.
12. Klein S M, Cohen G, Cederbaum A I, 1981. Production of formaldehyde during metabolism of dimethyl sulfoxide by hydroxyl radical-generating systems. Biochemistry. Oct 1;20(21):6006-12.
13. Rahman M, Islam M B, Biswas M, Alam A K, 2015. In vitro antioxidant and free radical scavenging activity of different parts of Tabebuia pallida growing in Bangladesh. BMC research notes. ;8(1):1-9.
14. Marcocci L, Maguire J, Droylefaix M T, Packer L, 1994. The nitric oxide-scavenging properties of *Ginkgo biloba* extract EGb 761. Biochemical and Biophysical Research Communication. 201(2):748-55.
15. Boora F, Chirisa E, Mukanganyama S, 2014. Evaluation of nitrite radical scavenging properties of selected Zimbabwean plant extracts and their phytoconstituents. Journal of Food Processing. 6;.
16. Mabry T J, Markham K R, Thomas M B, 1970. The ultraviolet spectra of isoflavones, flavanones and dihydroflavonols. InThe systematic identification of flavonoids Springer, Berlin, Heidelberg.pp. 165-226.
17. Tsimogiannis D, Samiotaki M, Panayotou G, Oreopoulou V, 2007. Characterization of flavonoid subgroups and hydroxy substitution by HPLC-MS/MS. Molecules. ;12(3):593-606.
18. Soubhye J, Chikh Alard I, Aldib I, Prévost M, Gelbcke M, De Carvalho A, Furtmüller P G, Obinger C, Flemmig J, Tadrent S, Meyer F, 2017. Discovery of novel potent reversible and irreversible myeloperoxidase inhibitors using virtual screening procedure. Journal of medicinal chemistry. 10;60(15):6563-86.
19. Heinecke J W, Li W, Francis G A, Goldstein J A, 1993. Tyrosyl radical generated by myeloperoxidase catalyzes the oxidative cross-linking of proteins. The Journal of clinical investigation. 91(6): 2866-72.
20. Hampton M B, Kettle A J, Winterbourn C C, 1998. Inside the neutrophil phagosome: oxidants, myeloperoxidase, and bacterial killing. Blood. 92(9): 3007-17.
21. Shao B, Oda M.N., Oram J F, Heinecke JW, 2009. Myeloperoxidase: an oxidative pathway for generating dysfunctional high-density lipoprotein. Chemical research in toxicology. 23(3): 447-54.
22. Pavithra K, Vadivukkarasi S, 2015. Evaluation of free radical scavenging activity of various extracts of leaves from Kedrostis foetidissima (Jacq.) Cogn. Food Science and Human Wellness. 1;4(1):42-6.
23. Lalitha V, Korah M C, Sengottuvel S, Sivakumar T 2015. Antidiabetic and antioxidant activity of resveratrol and vitamin-C combination on streptozotocin induced diabetic rats. Int J Pharm Sci.;7(9):455-8.
24. Nagmoti D M, Khatri D K, Juvekar P R, Juvekar A R, 2012. Antioxidant activity free radical-scavenging potential of Pithecellobium dulce Benth seed extracts. Free Radicals and Antioxidants. 2(2):37-43.
25. Turkoglu A, Duru M E , Mercan N, Kivrak I, Gezer K. 2007. Antioxidant and antimicrobial activities of Laetiporus sulphureus (Bull.) Murrill. Food Chemistry. 101(1): 267-73.
26. Sundaram K M, Nanthini UR, Yadav S A, Thangavel S I, 2015. Anti-oxidant and anti-microbial activities of synthetic 3-formyl, 7-flavonol intermediates obtained by microwave assisted technique. Int J Pharm Sci. 7:124-8.
27. Banerjee S, Chanda A, Ghoshal A, Debnath R, Chakraborty S, Saha R, Das A, 2011. Nitric Oxide Scavenging Activity Study of Ethanolic Extracts of from Two Different Areas of Kolkata. Asian J Exp Biol Sci. 2:595-9.

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