Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(4), 2724-2735 | ISSN:2251-6727

Synthesis, Characterization and Evaluation of Quercetin Derivatives for Anti-Microbial and Anti-Fungal Activity

Arbind Pal[1], Raj Bhushan Singh[1], Abhay kumar Dubey[2], Arvind Kumar Srivastava[1]*

1. Department of Pharmaceutical Chemistry, Shambhunath Institute of Pharmacy, Jhalwa, Prayagraj, Uttar Pradesh (India)211015
2. Department of Pharmaceutics, Shambhunath Institute of Pharmacy, Jhalwa, Prayagraj, Uttar Pradesh (India)211015

Corresponding Author: Arvind Kumar Srivastava[2]

Department of Pharmaceutical Chemistry, Shambhunath Institute of Pharmacy, Jhalwa, Prayagraj, Uttar Pradesh, (India).

(Received: 16 June 2025 Revised: 20 July 2025 Accepted: 19 August 2025)

KEYWORDS

Quercetin, Quercetin derivatives

ABSTRACT:

The study involves synthesis, characterization and evaluation of anti-microbial and anti-fungal activity for the derivatives of quercetin. The product to be synthesized was selected on the basis of SWISS ADME predictor. The characterization of drug and their synthesised products was done by determination of melting point, UV spectroscopy, FTIR spectroscopy, thin layer chromatography, Nuclear Magnetic Resonance study. The anti-microbial and anti-fungal studies were done with different concentrations of 12.5 mg/ml, 25mg/ml, and 50 mg/ml with derivative 1 and derivative 2 using Pseudomonas aeruginosa Aspergillus Niger strains. The drug with 50mg/kg shows potent anti-microbial and anti-fungal activity with effective inhibitory growth parameter.

1. INTRODUCTION

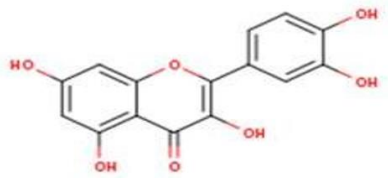
Heterocyclic chemistry involves use of hetero atoms in general chemistry in order to drug discovery and development of new compound. It includes heterocyclic compounds as well as bio-organic compounds like furan, pyrrole, thiophene, pyridine, pyrimidine, imidazole, benzimidazole, etc. The heterocyclic chemistry also has an important role in the study of characterization properties of compounds. So, it can also be defined as the chemistry that involves the synthesis, study of properties and study of significant role of compounds in development of new chemical compounds.(1). Quercetin, a natural compound found in many plants. It belongs to a group of substances called flavonoids, which have a specific structure. The structure of quercetin consists of three basic ring that is named as ring A, ring B and ring C. The new derivatives are derived by making modifications in the basic ring of the moiety.

This structure can be changed by adding or removing different parts, like hydroxyl, methoxyl, or glycosyl groups. These changes create various types of quercetin-related compounds. For example, adding glucose to quercetin makes isoquercetin, while adding galactose creates hyperoside. Other variations include attaching different sugars or sugar combinations to different parts of the quercetin molecule. Some compounds have methyl groups added, like tamirixetin and rhamnetin(2,3). There are also more complex forms with multiple sugar units attached. These different quercetin-based compounds can have unique properties and effects in nature and potentially in human health.

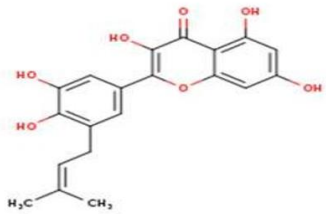
Journal of Chemical Health Risks

www.jchr.org

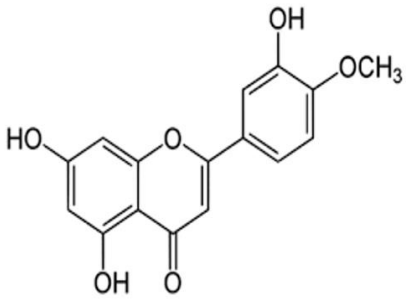
JCHR (2025) 15(4), 2724-2735 | ISSN:2251-6727



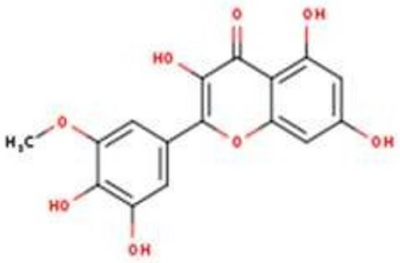
Quercetin 3'-Hydroxykaempferol



Uralenol 3,5,7,3',4'- Pentahydroxy-5'- isoprenylflavone



4'-O-Methyltaxifolin 3,5,7-trihydroxy-2-(3-hydroxy-4-methoxyphenyl)-2,3-dihydrochromen-4-one



8-methylquercetin

Anti-Microbial Properties

The antimicrobial properties of quercetin were studied and shows potent antimicrobial antibacterial antifungal activity. It is able to resist a wide range of microorganisms including broad spectrum and narrow spectrum microorganism's category.(4,5) The drug quotes team shows effect on wide range of microorganisms like salmonella species, E coli, Listeria, Mycobacterium, Streptococcus, pseudomonas species, bacillus subtilis, Salmonella Typhimurium, and aerobic bacteria's (6).

2. MATERIAL AND METHODOLOGY

Designing synthetic schemes by computational studies: ADME PREDICTION

The Swiss ADME Predator is a scientific tool that is used to predict the absorption distribution metabolism and excretion of drug using software design. It predicts the structure, and all the feasible chemical properties of the given structure that is used to assess the derivatives of a compound, to collect information about the drug with its derivatives and to characterize the percentage of similarity of structure with respect to its primary ring(7,8). It requires either structure of the compound or SMILES (A form of code that justifies the structure of a compound). (9).

Evaluation and characterization of Quercetin.

UV-Visible spectroscopy

To measure quercetin, we first made a strong solution by mixing 0.1g of quercetin with 100ml of ethanol. This gave us a concentration of 1000µg/ml. Then, we took a tiny bit of this solution, just 0.1ml, and added more ethanol to make it 100ml total. This step made the solution much weaker, with a concentration of 10µg/ml(10,11).

Melting point –It is the temperature under which the melting of solid product occurs. The value is in the range which justifies that the melting point of that melting certain product lies between the described point. M.P. of Quercetin, examined with help of G-Lab apparatus(12).

FTIR spectroscopy

The IR spectrum of Quercetin mixed with dried KBr disc was studied using a Perkin-Elmer Infrared

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(4), 2724-2735 | ISSN:2251-6727

Spectrophotometer. This method helps scientists understand the structure of Quercetin by looking at how it interacts with light. The KBr disc is used because it doesn't interfere with the results. When the light hits the Quercetin sample, it creates a pattern (13).

1.1. Synthesis of some novel Quercetin derivatives:

Scheme: 1- 3' O methylation of quercetin to 3,5,7-trihydroxy-2-(4-hydroxy-3 methoxyphenyl)chromen-4-one.

Quercetin (3 gram) mixed with 1.63 gm of sodium acetate, diluted in 20 ml of acetic anhydride, refluxed for 18 hours. Cooled the mixture followed by addition of 90 ml of dichloromethane. Filtered and dried by using anhydrous sodium sulphate. The dried product was reacted with potassium iodide (0.32 gm) followed by reaction with 0.9 ml of benzyl chloride in 60 ml of dry acetone at 45^0C for 24 hours. The above synthesized compound was using dichloromethane, washed with brine and water. The filtered product was reacted with 1.56 gm of potassium iodide and separated by using access of methyl iodide using chromatographic run. The obtained content was purified by using the same technique.

Scheme-2: 4' O methylation of quercetin to synthesize 3,5,7-trihydroxy-2-(3-hydroxy-4 methoxyphenyl)chromen-4-one.

354 mg of dichlorodiphenylmethane was mixed with 302 mg of quercetin in 20 ml of diphenyl ether with continuous stirring. The mixture was heated at 175^0C for 30 minutes followed by cooling to room temperature. Further reacted with 1.28 ml of chloromethyl methylether and 2.45 gm of potassium carbonate. The mixture was filtered & filtrate, added 10 ml of ethanol and 10 ml of THF with 2mg of 10% lead. After 8 hours, the product was filtered, 0.019 ml of iodomethane reacted with 20 ml DMF. The resulting product was divided into 100 ml of ethyl acetate and 100 ml of water. The ethyl acetate layer was dried using MgSO4, followed by filtration. Added 1 ml of HCL, stirred with 5 ml of dichloromethane at room temperature for 6 hours. Filtered with water washed with brine and solidified by using MgSO4.

IN VITRO ANTIBACTERIAL ACTIVITY

The antibacterial activity of Quercetin derivatives was tested using a special method called Microtitre Broth dilution. This was done in small plates with 96 wells. The compounds were mixed with different amounts of liquid to make solutions of 12.5, 25, and 50 mg/mL. They tested these against a tough bacterium called Carbapenam resistant Pseudomonas aeruginosa (MCCB0057). Put the solutions in the wells along with some special liquid (Mueller-Hinton broth), bacteria, and a colour-changing substance (TTC). They then kept the plates warm for 18 hours. If the wells turned pink, it meant the bacteria were growing. If there was no color, it meant the bacteria were not growing. They also had two special wells: one without the test compound and one with Quercetin derivatives. The lowest amount of the compound that stopped the bacteria from growing was called the Minimum Inhibitory Concentration. This test helped the scientists figure out how well the Quercetin derivatives worked against the tough bacteria.

IN VITRO ANTIFUNGAL ACTIVITY

Aspergillus niger (MCCB0201) strains were screened for current study. The fungi were conserved, grown and sub cultured at 38°C on Peptone plates for 48 hours.

Prepared different strengths of a special substance made from Quercetin. They used 12.5, 25, and 50 mg/mL of this substance. They put small amounts of these into tiny wells on a special plate. They also added some fungus mixture and a color-changing chemical. They left this plate in a warm place for 24 hours, gently shaking it. After waiting, they looked at the wells. If a well-turned pink, it meant the fungus was growing. If there was no color, it meant the fungus couldn't grow. They wanted to find out how much of their special substance was needed to stop the fungus from growing. This amount is called the Minimum Inhibitory Concentration. They looked for the well with no colour to figure this out. They decided that when 90% of the fungus couldn't grow, they had found the right amount of their special substance.

3. RESULT DISCUSSION

The physical characterization of drug was done and it was found to be powdered form with light yellow colour. The melting point of drug was determined and was found to be 316^0C.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(4), 2724-2735 | ISSN:2251-6727

Thin Layer Chromatography: The thin layer chromatography of quercetin was done and Rf value was found to be 0.59**.**

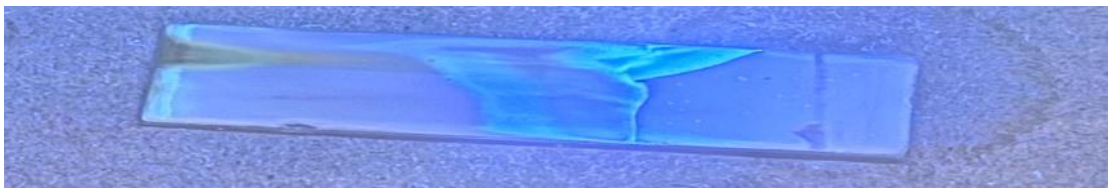
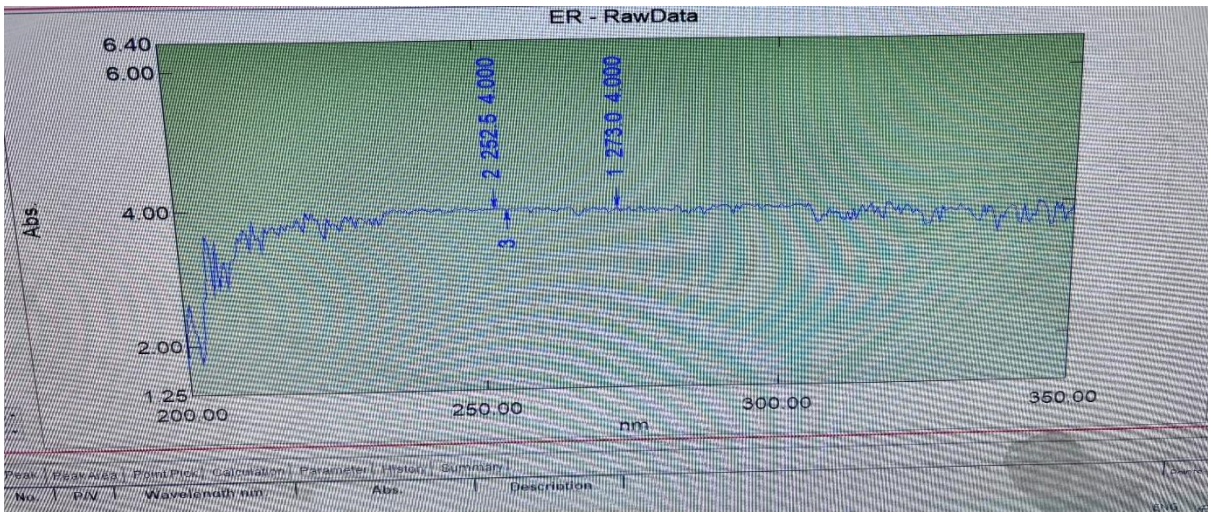


Figure 1: Showing TLC of quercetin

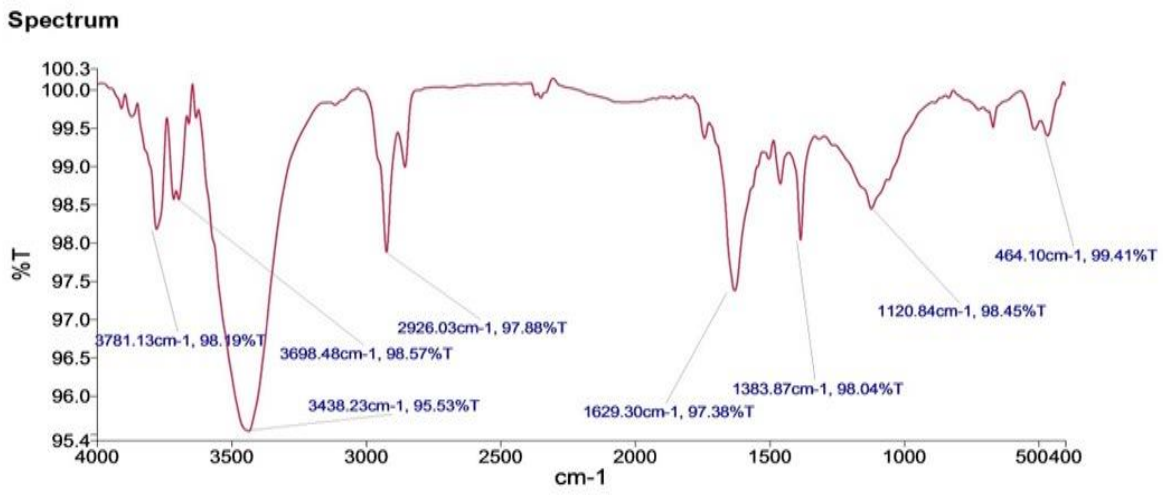
UV spectroscopy

Absorbance of Quercetin is determined under UV spectrometer and it was found to be 273 nm.



Graph 1: Showing UV spectroscopy of Quercetin.

FTIR Spectroscopy of Quercetin



Graph 2: Showing FTIR spectroscopy of Quercetin

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(4), 2724-2735 | ISSN:2251-6727

ADME PROFILE OF QUERCETIN DERIVATIVES

Table 1: ADME profile of quercetin derivatives

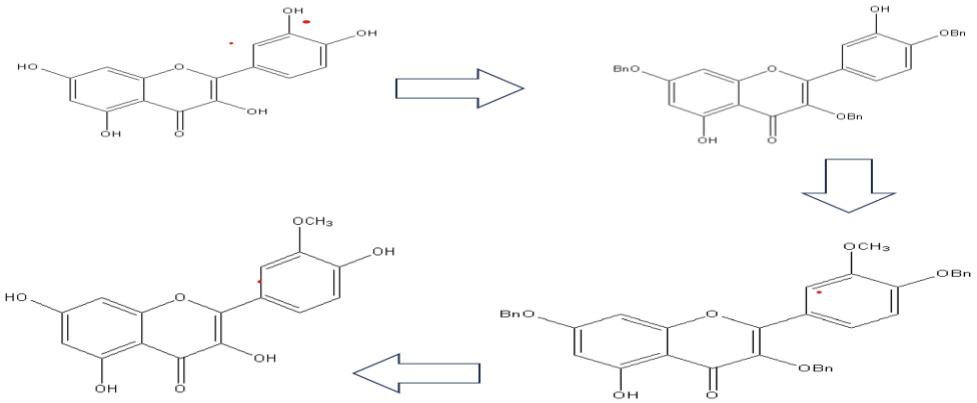
S.No.	ID	GI absorption	BBB permeant	PGP substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor
1	CHEMBL 1173475	High	No	No	Yes	No	No	Yes	Yes
2	CHEMBL 113833	High	No	No	Yes	No	Yes	Yes	No
3	CHEMBL 457261	Low	No	No	Yes	No	No	No	No
4	CHEMBL 463452	High	No	No	Yes	No	Yes	Yes	No
5	CHEMBL 2260151	Low	No	No	Yes	No	No	Yes	Yes
6	CHEMBL 382937	High	No	No	Yes	No	No	Yes	Yes
7	CHEMBL 193059	High	No	No	Yes	No	Yes	Yes	No
8	CHEMBL 3617858	Low	No	No	Yes	No	No	No	No
9	CHEMBL451709	High	No	No	Yes	No	No	No	No
10	CHEMBL 458762	Low	No	No	Yes	No	No	No	No
11	CHEMBL 323712	Low	No	No	Yes	No	No	No	No
12	CHEMBL 164	Low	No	No	Yes	No	No	No	Yes
13	CHEMBL 465155	Low	No	No	Yes	No	No	Yes	Yes
14	CHEMBL451709	High	No	No	Yes	No	No	No	No
15	CHEMBL 312163	High	No	No	Yes	No	No	Yes	Yes
16	CHEMBL 515360	Low	No	No	No	No	No	No	No

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(4), 2724-2735 | ISSN:2251-6727

17	CHEMBL502782	Low	No	Yes	No	Yes	No	No	No
18	CHEMBL413552	Low	No	No	Yes	No	No	No	Yes
19	CHEMBL470848	High	No	No	Yes	No	No	Yes	Yes
20	CHEMBL1935385	High	No	Yes	Yes	No	No	Yes	Yes

Scheme of Synthesis for derivative - 1

3' O methylation of quercetin to 3,5,7-trihydroxy-2-(3-hydroxy-4 methoxyphenyl)chromen-4-one.

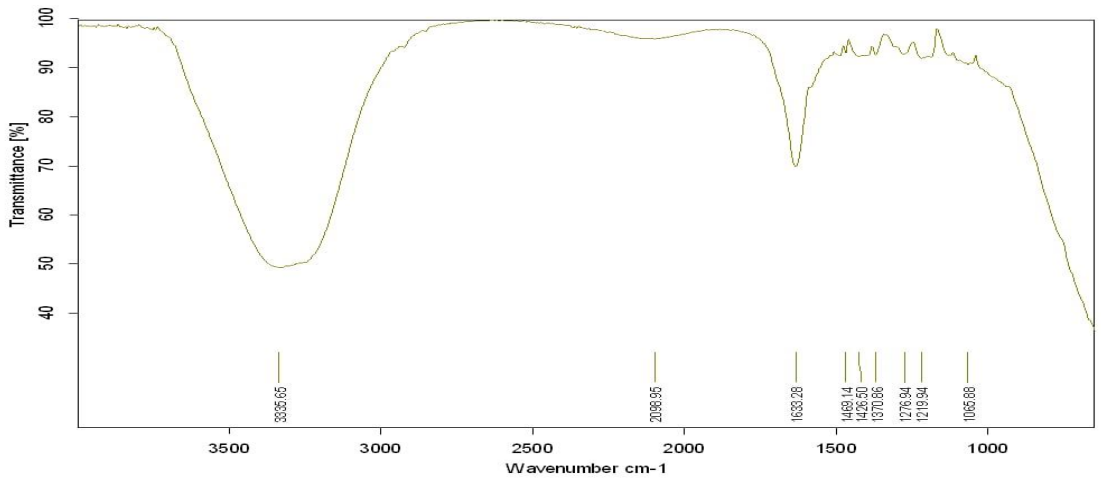


Characterization of Derivative-1

The physical nature of drug was found to be light yellow, having melting point of 793^{0}C.

The Rf value of sample was found to be 0.62.

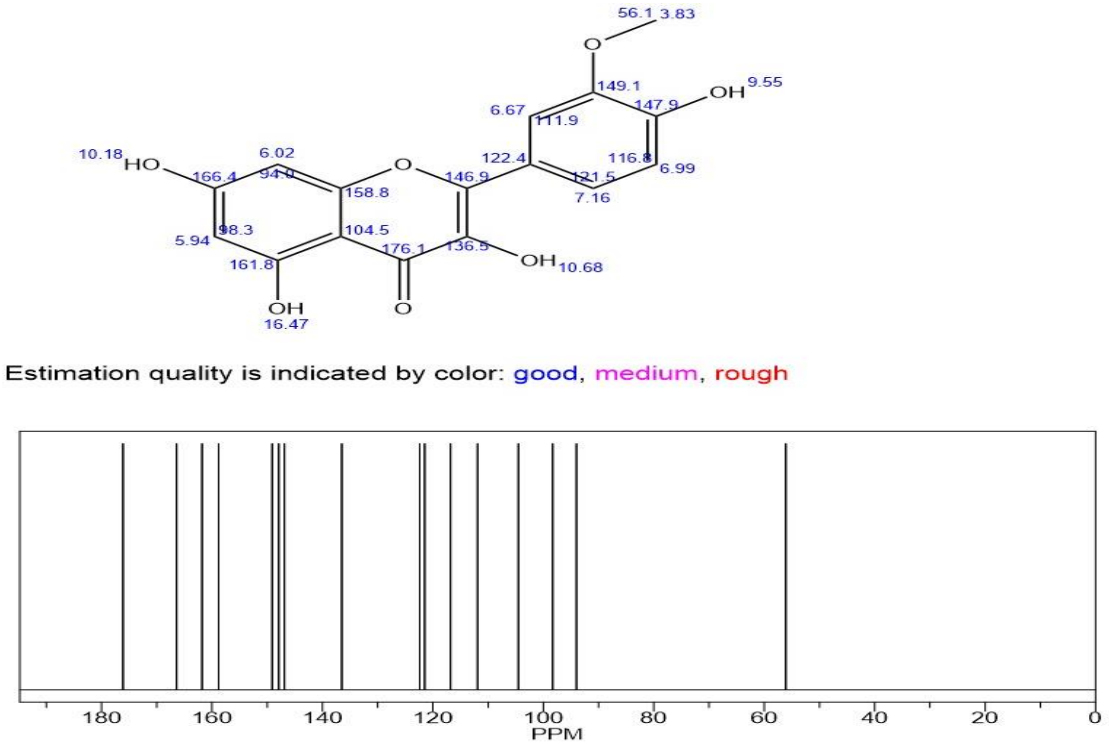
Fourier transform infrared spectroscopy (FT-IR).



Graph 3: Fourier transform infrared spectroscopy (FT-IR) of quercetin derivative 1

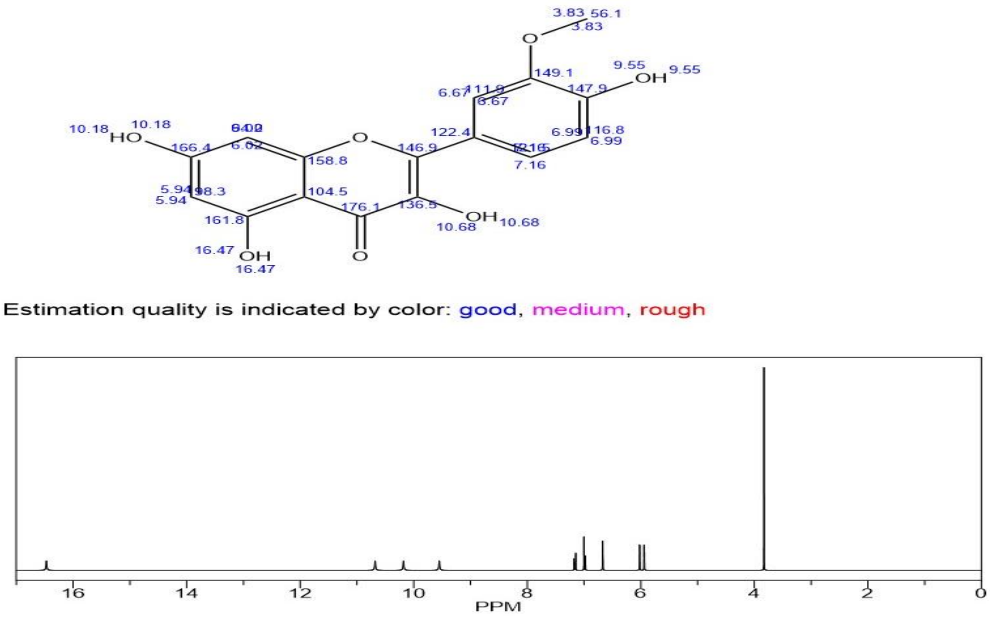
Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(4), 2724-2735 | ISSN:2251-6727

C13 NMR of Derivative -1



Graph 4: Showing C13 NMR peaks of synthesized derivative 1.

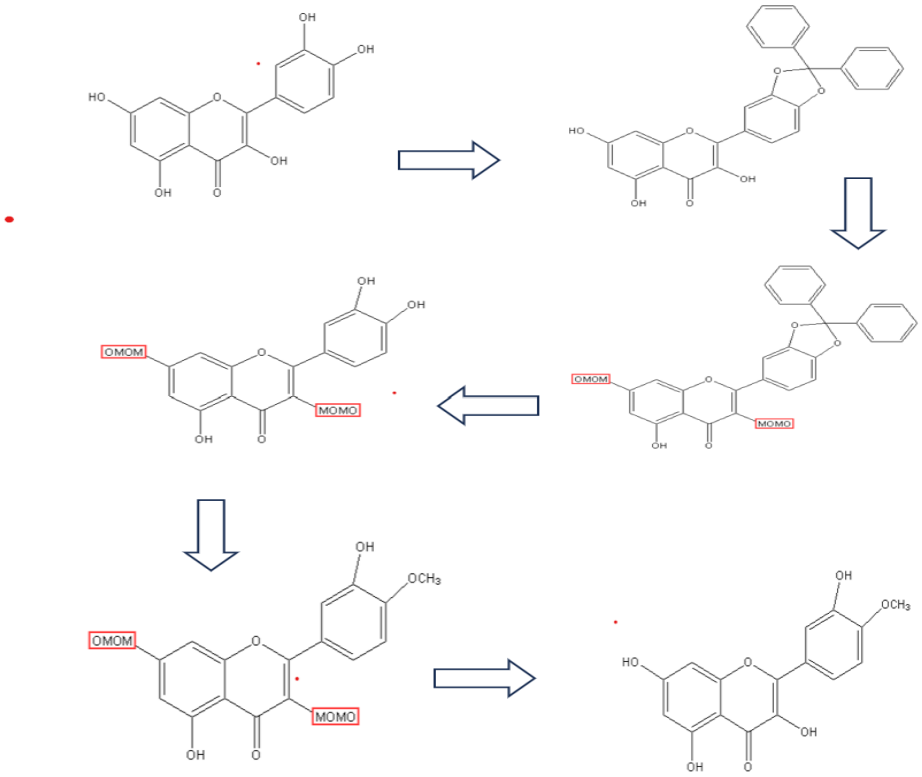
H1 NMR of Derivative -1



Graph 5: Showing H1 NMR peaks of synthesized derivative 1.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(4), 2724-2735 | ISSN:2251-6727

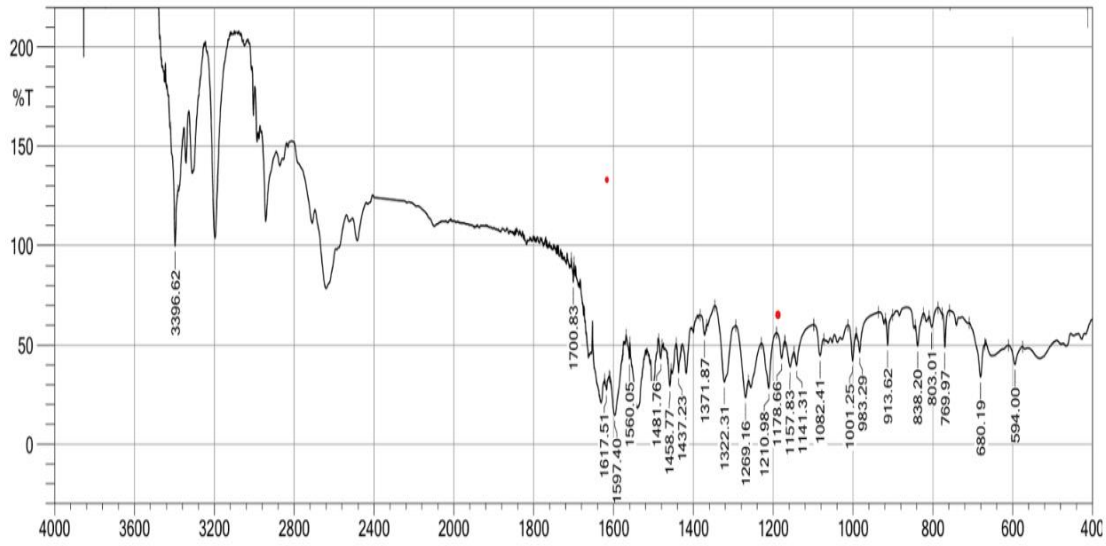
Scheme of Synthesis – for DERIVATIVE – 2



The physical nature of drug was found to be light green, having melting point of 813^{0}C.

The Rf value of sample was found to be 0.58.

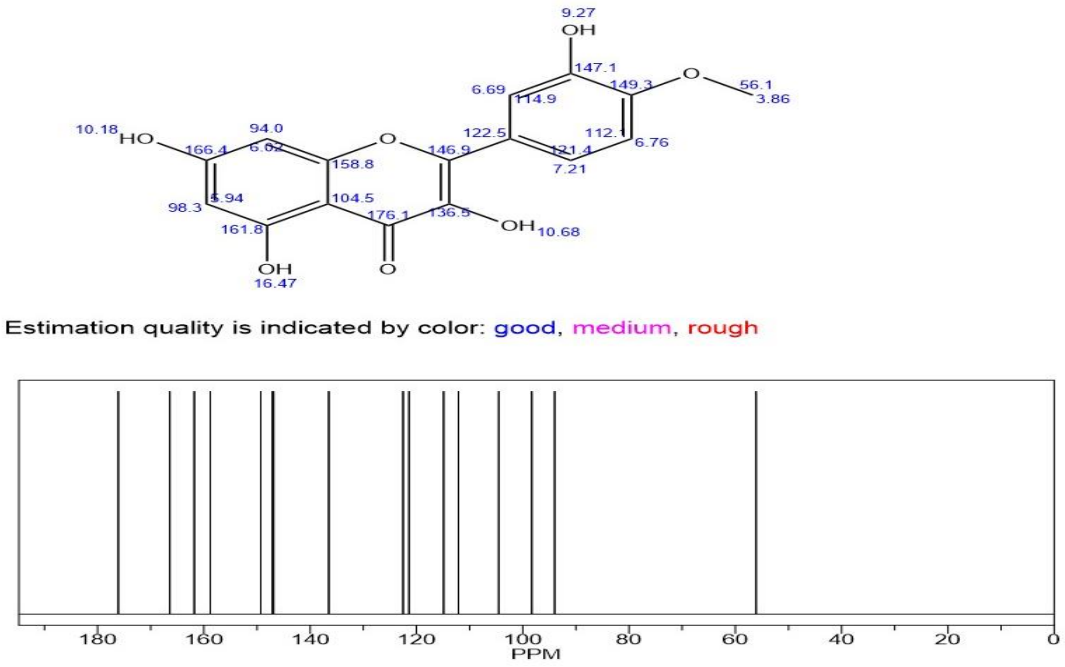
Fourier transform infrared spectroscopy (FT-IR).



Graph 6: Fourier transform infrared spectroscopy (FT-IR) of quercetin derivative 1

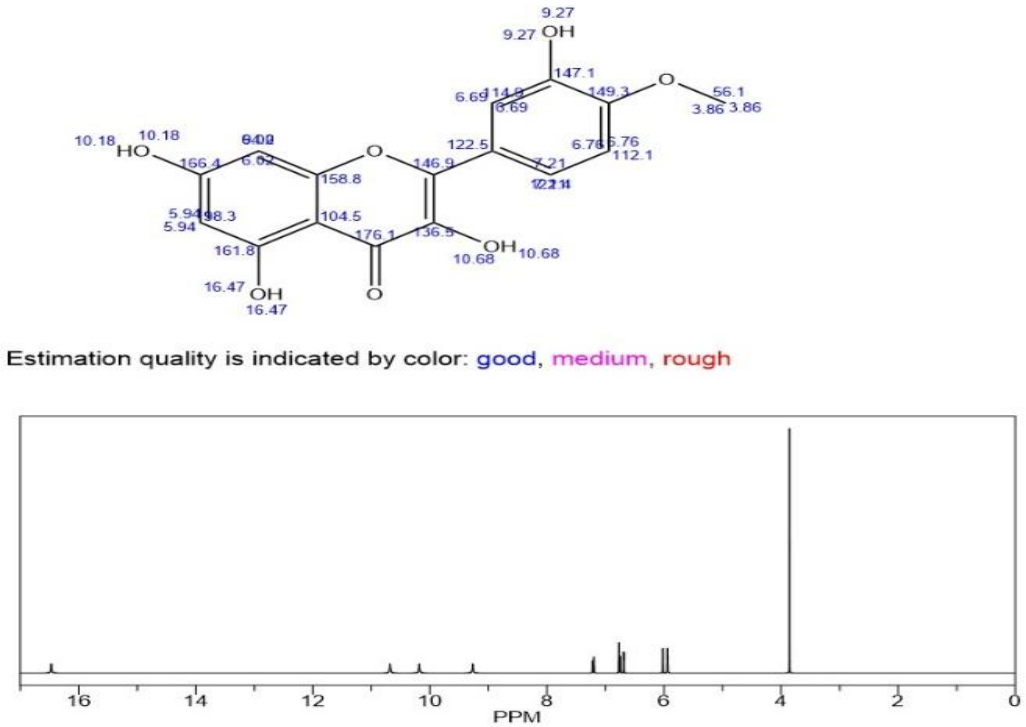
Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(4), 2724-2735 | ISSN:2251-6727

C13 NMR of Derivative -2



Graph 7: Showing C13 NMR peaks of synthesized derivative 2.

H1 NMR of Derivative -2



Graph 8: Showing H1 NMR peaks of synthesized derivative 2.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(4), 2724-2735 | ISSN:2251-6727

Evaluation of Anti-bacterial activity

All results were observed after 90 minutes of dosing.

Table 2: showing anti-bacterial activity of derivative - 1

Strain	**After culture**	**Dosing with derivative - 1**		
	After culture	**12.5 mg/ml**	**25 mg/ml**	**50mg/ml**
Pseudomonas aeruginosa	Appears as pink colour	Pink colour remains 50%	Pink colour remains 20%	Pink colour remains 10%

Table 3: showing anti-bacterial activity of derivative - 2

Strain	**After culture**	**Dosing with derivative - 2**		
	After culture	**12.5 mg/ml**	**25 mg/ml**	**50mg/ml**
Pseudomonas aeruginosa	Appears as pink colour	Pink colour remains 45%	Pink colour remains 15%	Pink colour remains 8%

Evaluation of Anti-fungal activity

Table 4: showing anti-fungal activity of derivative – 1

Strain	**After culture**	**Dosing with derivative - 1**		
	After culture	**12.5 mg/ml**	**25 mg/ml**	**50mg/ml**
Aspergillus Niger	Appears as pink colour	Pink colour remains 50%	Pink colour remains 20%	Pink colour remains 10%

Table 5: showing anti-fungal activity of derivative - 2

Strain	**After culture**	**Dosing with derivative - 2**		
	After culture	**12.5 mg/ml**	**25 mg/ml**	**50mg/ml**
Aspergillus Niger	Appears as pink colour	Pink colour remains 50%	Pink colour remains 20%	Pink colour remains 9%

Figure 2: Showing stages of culture media during bacterial growth, after 50mg/ml of dosing with derivative 1 and derivative 2

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(4), 2724-2735 | ISSN:2251-6727

4. CONCLUSION

The quercetin was characterized on the basis of melting point, uv spectroscopy, FTIR spectroscopy and thin layer chromatography. The obtained result is shown as the Rf value of quercetin was found to be 0.59 that is equivalent to Rf value of quercetin which proves that the given drug sample is quercetin. The melting point of quercetin was calculated and it was found to be 316^0C that is in the range of 310-318^0C. The UV spectroscopy of drug sample was done using ethanol as solvent. The peak was obtained at 273 nm which confirm that the drug sample is quercetin. On the basis FTIR spectroscopy, the obtained peaks in the spectra show confirmation of quercetin. 20 derivatives having % similarity >90% are evacuated, and their structures were studied which is further used in ADME predictor using SWISS ADME to predict the absorption, distribution, metabolism and excretion properties of drug. The melting point and TLC of derivative – 1 was found to be 793^0C and 0.62 respectively. The C13 NMR and H1 NMR peaks confirm the synthesis of derivative-1. FTIR spectroscopy was done to evaluate the vibrational frequencies of the compound. The melting point and TLC of derivative – 2 was found to be 813^0C and 0.59 respectively. The C13 NMR and H1 NMR peaks confirm the synthesis of derivative-2. The anti-microbial and anti-fungal was done using Pseudomonas aeruginosa and Aspergillus Niger with both the synthesized derivatives. The obtained results show 90% of inhibitory effect with 50mg/ml of dosing.

5. REFERNECES

1. Alvarez-Builla J, Vaquero JJ, Barluenga J, editors. Modern Heterocyclic Chemistry. Wiley; 2011.

2. Paulke A, Eckert GP, Schubert-Zsilavecz M, Wurglics M. Isoquercitrin provides better bioavailability than quercetin: comparison of quercetin metabolites in body tissue and brain sections after six days administration of isoquercitrin and quercetin. Pharmazie. 2012 Dec;67(12):991–6.

3. Kajbafvala A, Salabat A, Salimi A. Formulation, characterization, and *in vitro/ex vivo* evaluation of quercetin-loaded microemulsion for topical application. Pharm Dev Technol. 2018 Sep 14;23(8):741–50.

4. Carrillo-Martinez EJ, Flores-Hernández FY, Salazar-Montes AM, Nario-Chaidez HF, Hernández-Ortega LD. Quercetin, a Flavonoid with Great Pharmacological Capacity. Molecules. 2024 Feb 25;29(5):1000.

5. Odabaş Köse E, Koyuncu Özyurt Ö, Bilmen S, Er H, Kilit C, Aydemir E. Quercetin: Synergistic Interaction with Antibiotics against Colistin-Resistant Acinetobacter baumannii. Antibiotics. 2023 Apr 12;12(4):739.

6. Grande F, Parisi OI, Mordocco RA, Rocca C, Puoci F, Scrivano L, et al. Quercetin derivatives as novel antihypertensive agents: Synthesis and physiological characterization. European Journal of Pharmaceutical Sciences. 2016 Jan;82:161–70.

7. Sączewski J, Popenda Ł, Fedorowicz J. In Silico SwissADME Analysis of Antibacterial NHC–Silver Acetates and Halides Complexes. Applied Sciences. 2024 Oct 2;14(19):8865.

8. Mvondo JGM, Matondo A, Mawete DT, Bambi SMN, Mbala BM, Lohohola PO. In Silico ADME/T Properties of Quinine Derivatives using SwissADME and pkCSM Webservers. Int J Trop Dis Health. 2021 Aug 3;1–12.

9. Bakchi B, Krishna AD, Sreecharan E, Ganesh VBJ, Niharika M, Maharshi S, et al. An overview on applications of SwissADME web tool in the design and development of anticancer, antitubercular and antimicrobial agents: A medicinal chemist's perspective. J Mol Struct. 2022 Jul;1259:132712.

10. Adeeyinwo CE, Okorie NN. Basic Calibration of UV/ Visible Spectrophotometer. Vol. 2, International Journal of Science and Technology. 2013.

11. Adeeyinwo CE, Okorie NN. Basic Calibration of UV/ Visible Spectrophotometer. Vol. 2, International Journal of Science and Technology. 2013.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(4), 2724-2735 | ISSN:2251-6727

12. CHAPTER 6 RESULTS AND DISCUSSION 6.1 RESULTS OF FORMULATION AND EVALUATION OF GEL LOADED WITH FLURBIPROFEN MICROSPONGES 6.1.1 Results of Preformulation studies of Flurbiprofen (FP) 6.1.1.1 Results of melting point of FP Table 6.1 Results of Melting Point of FP.

13. Chen Y, Furmann A, Mastalerz M, Schimmelmann A. Quantitative analysis of shales by KBr-FTIR and micro-FTIR. Fuel. 2014;116:538–49.