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Short Communication

Synthesis and Physico-Chemical Analysis of 3-{[(3, 4-Dimethoxy-Phenyl)-Phenylamino-Methyl]-Amino}-2-Phenyl-Quinazolin-4(3h)-One

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Abstract

Medicinal chemistry as practiced encompasses both definitions, but finding the biochemical pathways through which drug exert their beneficial effects has become a dominating activity of the medicinal chemist and biologist while searching for ahead on a new drug or doing research on a pre-clinical drug candidate. Heterocyclic chemistry is the branch of chemistry dealing with the synthesis, properties, and applications of heterocyclics. Heterocyclic chemistry comprises at least half of all organic chemistry research worldwide. In particular, heterocyclic structures form the basis of many pharmaceutical, agrochemical and veterinary products. Quinazolinone has been considered as a magic moiety possessing myriad spectrum of medicinal activities. Diversity of biological response profile has attracted considerable interest of several researchers across the globe to explore this skeleton for its assorted therapeutic significance. By using different synthetic methods new quinazolinone derivatives were synthesized and characterized by physic-chemical analysis. Quinazolinone is a lead nucleus for future developments to get effective compounds.

Keywords: Quinazolinone, anthranilic acid, quinazoline, aniline, 4-Hydroxy benzaldehyde, 2-phenyl-1,3-benzoxazin-4-one, Ethanol.

Introduction

Medicinal chemistry and pharmacology both are concerned with mode of action and SAR of drugs. However, this kind of overlap facilities productive interactions in research. Any of a class of organic compounds whose molecules contain one or more rings of atoms with at least one atom being an element other than carbon, most frequently oxygen, nitrogen, or sulfur is called heterocyclic compounds. Heterocyclic chemistry is the branch of chemistry dealing with the synthesis, properties, and applications of heterocyclics[1, 2].

Heterocyclic chemistry comprises at least half of all organic chemistry research worldwide. In particular, heterocyclic structures form the basis of many pharmaceutical, agrochemical and veterinary products. The word hetero means “different from carbon and hydrogen”. Many heterocyclic compounds are biosynthesized by plants and animals are biologically active. Some heterocyclic compounds are fundamentals of life, like haeme derivatives in blood and chlorophyll essential for photosynthesis in plants. Also the DNA and RNA are containing heterocyclic[3, 4].

Dyestuffs of plant origins include indigo blue used to dye jeans. Several heterocycles are the basic structure nucleus for nicotine, pyridoxine, cocaine, morphine etc. Quinazolinone has been considered as a magic moiety possessing myriad spectrum of medicinal activities. Diversity of biological response profile has attracted considerable interest of several researchers across the globe to explore this skeleton for its assorted therapeutic significance[5].

Material and Methods

Synthesis of Anthranilic acid: Prepare a solution of 30 gm of sodium hydroxide in 120 ml of water. Cool to 0^0C.add 0.16 ml of bromine and shake until all the bromine gets reacted. Cool to 0^0C. Prepare a solution of 22 gms of NaOH in 80 ml of water. Add finely powdered phthalimide (0.163 mol) in one portion to the cold sodium hypobromite solution in the form of a thin paste. Shake vigorously until a clear yellow solution is obtained. Add the prepared NaOH rapidly, heat to 80^0C for 2 minutes. Cool in ice and add concentrated hydrochloric acid slowly with stirring until the solution is just neutral. Precipitate anthranilic acid completely by gradual addition of glacial acetic acid. Filter and recrystallise from hot water[6].

Synthesis of 2-phenyl-1, 3-benzoxazin-4-one (II): Anthranilic acid (0.1mol) was dissolved in 50 ml of pyridine. To this benzoyl chloride (0.2 mol) was added drop wise with constant stirring at low temperature. When the addition of benzoyl chloride was completed, mixture was treated with 10% sodium bicarbonate solution (15 ml). After the effervescence ceased, mixture was filtered and washed repeatedly with water to remove inorganic materials. The crude drug thus obtained was recrystallised from ethanol[7, 8].

Synthesis-of 3-amino-2-phenyl quinazolin-4-(3H)-one (III): An equimolar (0.01 mol) mixture of benzoxazine and hydrazine hydrate was refluxed for 6hrs with 10ml of ethanol. The mixture was cooled to room temperature and poured into crushed ice, filter and then washed with water. The solid thus obtained was recrystallised from ethanol[9].

Synthesis of 3-{[(3, 4-Dimethoxy-phenyl)-phenylamino-methyl]-amino}-2-phenyl-3H-quinazolin-4-one (IV): An equimolar (0.01 mol) mixture of quinazoline, aniline (aromatic primary amine) and aldehyde was refluxed for 6hrs with 10ml of ethanol in acidic condition. The mixture was cooled to room temperature and poured into crushed ice, filter and then washed with water. The solid thus obtained was recrystallised from ethanol[10]

Determination of Melting Point: The normal melting point of a solid is defined as the temperature at which the solid and liquid are in equilibrium at a total pressure of 1 atmosphere. There are several methods by which melting points can be determined, and the choice of method depends mainly upon how much material is available[11].

Capillary Melting Points: Capillary melting points, either in an oil bath or a melting-point apparatus, are most often used for the determination of the melting point of a solid. A few crystals of the compound are placed in a thin walled capillary tube 10-15 cm long, about 1 mm in inside diameter, and closed at one end. The capillary, which contains the sample, and a thermometer are then suspended so they can be heated slowly and evenly. The temperature range over which the sample is observed to melt is taken as the melting point[12].

Thin Layer Chromatography: Thin layer chromatography was carried out over plates (20cm×5cm) coated with silica gel – G 13 % containing calcium sulphate as binder**.**

Principle: When a mixture of compounds is spotted on a TLC plate and development with a suitable solvent system the compound which are not strongly adsorbed move up along with a solvent. Those which are more strongly adsorbed more or less rapidly get separated due to different rates of migration on the layer[13].

Preparation of Thin layer chromatographic plates: 50gms of silica gel-G was weighed out and shaken to a homogenous suspension with 100 ml of distilled water for 90 seconds. This suspension was poured in to a TLC applicator which was adjusted to 0.25mm thickness. Twenty carrier plates (20cm×5mm) were laid together in a row on a template and coated with a silica gel-G by drawing the applicator. The plates were allowed to dry at room temperature and then dried at 110^0c for 30min, in hot air oven for activation. The dry plates were stored in desiccators and used whenever required[14, 15].

Results and Discussion

The present study explains the synthesis and characterization of new quinazolinone derivative i.e., 3-{[(3, 4-Dimethoxy-phenyl)-phenylamino-methyl]-amino}-2-phenyl-3H-quinazolin-4-one.
To study the structural activity relationship and to optimize the structure. The purity of the synthesized quinqzoline derivative was checked by thin layer chromatography (TLC) and R_f value was recorded.

Conclusion

By this study concluded that to find the structure-activity relationship and to optimize the structure of the synthesized quinazolinone derivative i.e., 3-{[(3, 4-Dimethoxy-phenyl)-phenylamino-methyl]-amino}-2-phenyl-3H-quinazolin-4-one.
The compound was characterized by physicochemical analysis, the purity of the compound was checked by TLC and it produces good yield.

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Reference

1. Gabriel Schmidt D.S., Synthesis of 5- chloro-2- methyl- 3-(5- methylthiazol-2-yl)-4(3H) quinazolinone and related compounds with potential biological activity*, Journal of Heterocyclic Chemistry,* **37,** 725-729 **(2000)**
2. Weddige J., Prakt, Synthesis and Biological screening of some heterocyclic derivatives of quinazolinones. *Journal of Organic* Chemistry, **36(11),** 141 **(2005)**
3. Mandal Subhash C. and Maity Tapan K., Journal *of Ethnopharmacology,* **72**, 87-92 **(2003)**
4. Indian Pharmacopoeia, Ed3, Delhi, The controller of publications, 105-107 **(1996)**
5. Joshi Dharti, Harish G. and Parekh B., H. Synthesis of 2, 4-aryl substituted quinazoline 4(3H) one, .*Journal of Medicinal* Chemistry. **3**, 169 **(2008)**
6. Chen K., Wang K. and Kirichian A.M., *et al.,* in silico design, synthesis, and biological evaluation of quinazolinone derivatives for alkaline phosphatase-mediated cancer diagnosis and therapy, *Molicular cancer therapy*, **5(12),** 3001-13 **(2006)**
7. Andotra C.S., Langer T.C. and Sumita D., Biological activity of some Quinazoline and quinazoline derivatives, *Indian Journal of Pharmaceutical Science,* **55**, 19-24 **(2011)**
8. Kunes J., Bazant J., Pour M., Waisser K., Slosarek M., Janota J., Synthesis of quinazoline derivatives with antitubercular activity, *IL Farmaco,* **55**, 725-729 **(2012)**

9. Minhua Zhou, Honggang Wang, Suolangjiba, Junping Kou and Boyang Y. *Journal of Ethnopharmacology*, **117**, 345-350 **(2008)**

10. Li Jiarong *et.al.* A new and facile synthesis of quinazoline-2, 4(1*H*,3*H*)-diones *Journal of Medicinal* Chemistry, **11**, 1193-96 **(2009)**

11. Padmaja A., Payani T., Dinneswara Reddy G. and Padmavathi V., Synthesis, antimicrobial and antioxidant activities of substituted pyrazoles, isoxazoles, pyrimidine and thioxopyrimidine derivatives, *Eur. J. Med. Chem*., **44**, 4557 4566 **(2009)**

12. Vogel's Textbook of Practical Organic Chem. 5th Ed., 1016, E.L.B.S., **(1996)**

13. Yadav P. and Purohit N.V., Synthesis and Microbial studies of some new Oxygen Heterocycles, *Der Pharmacia Lettre*, **4**, 565-570 **(2012)**

14. Hlavka J.J., Bitha P., Lim Y.I. and T. Stromeyer T.,Reactions of 2,3-diamino-4(3*H*)- pyrimidinones, *J.Heterocycl. Chem.*, **22,** 1317 **(1985)**

15. Seki T. and Iwanami Y., Reaction products of dialkyl acetylenedicarboxylates with 2,3- diaminopyridine, *J.Heterocycl. Chem.*, **32**, 1071 **(1995)**

16. Ayhan-Kilcigil G., antifungal properties of some benzimidazole derivatives, *Turky-Journal of Chemistry.,* **30**, 223 **(2006)**

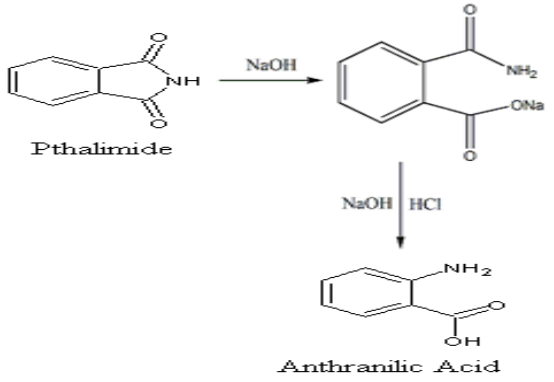

Figure-1

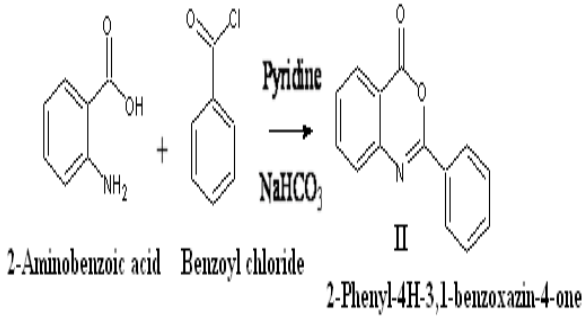

Figure-2

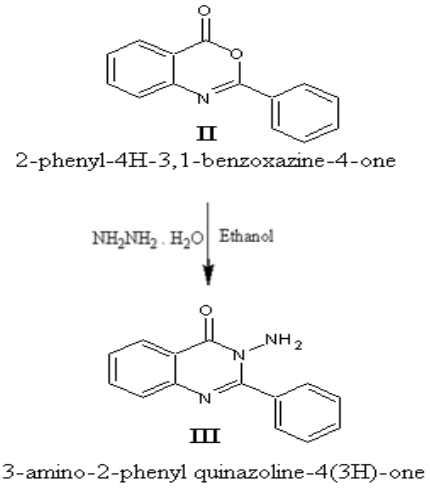

Figure-3

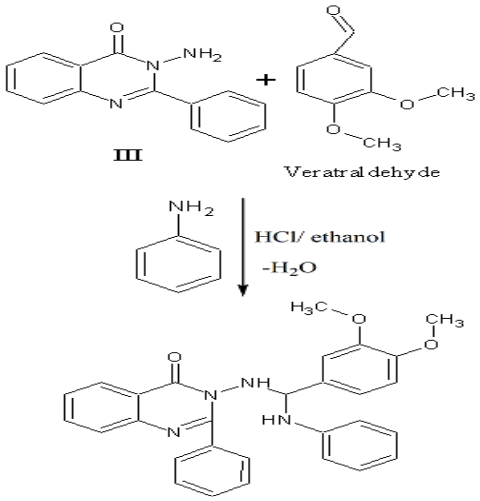

Figure-4

Physical and analytical data of synthesized compounds

Table-1

S.no	Compound	Mol. Formula	% Yield (w/w)
1.	I	$C_7H_7NO_2$	61.91%
2.	II	$C_{14}H_9NO_2$	59.30%
3.	III	$C_{14}H_{11}N_3O$	85.15%
4.	IV	$C_{29}H_{26}N_4O_3$	70.06%

Table-2

S.no	3-{[(3,4-Dimethoxy-phenyl)-phenylamino-methyl]-amino}-2-phenyl-3H-quinazolin-4-one	
1	Mol. Formula	$C_{29}H_{26}N_4O_3$
2	Mol. weight	478.55
3	Melting Point	62^oC
4	% Yield	70.06%
5	R_f Value	0.81