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Conglomerate and Analgesic Activity of 6-bromo-2-(o-aminophenyl)-3-amino-Quinazolin-4(3H)-one from 6-bromo,2-(o-aminophenyl)-3,1-benzoxazin-4(3H)-one.

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Abstract:

Introduction: Quinazolinone by–product disclosed various curative characteristics such as analgesic, anti-inflammatory and anticancer activities, as well as antimicrobial activity. These heterocycles are beneficial intermediates in organic synthesis. **Methods/Experimental:** The compound, 6-bromo,2-(o-aminophenyl)-3,1-benzoxazin-4(3H)-one(1) was integrated by dissolving 5-bromo anthranillic acid in 100 ml of pyridine. To this reaction mixture o-amino benzoyl chloride stirring at room temperature for 30 minutes this was refluxed with 75 mL of hydrazine hydrate for 3 hrs at 120-130^{0}C. the reaction mixture was allowed to cool to room temperature to give 6-bromo-2-(o-aminophenyl)-3-amino-Quinazolin-4(3H)-one **(2).** These Compounds were evaluated for their analgesic activity using Acetic acid induced model. **Study Design:** This study was experimentally design and the analgesic activity was evaluated

using Acetic acid induced model. **Result:** The compounds synthesized were evaluated pharmacologically for their in-vivo analgesic activities by acetic acid induced writhing in mice. The two scrutinized compounds exhibited significant analgesic activity in the range of 61.33 - 83.18% in comparison to control. **Conclusions:** From our findings, compound 2 synthesized have higher analgesic activities as compared to indomethacin a standard analgesic drug.

Keywords Analgesic activity; Coglomerate; Quinazolinone derivatives; 6-bromo-2-(o-aminophenyl)-3-amino-Quinazolin-4(3H)-one; 6-bromo,2-(o-aminophenyl)-3,1-benzoxazin-4(3H)-one.

Introduction

Different types of Quinazolinones disclose a capacious spectrum of organic activeness including anticancer[1], antimicrobial[2,5], anticonvulsant[3], antitubercular[4], anti-inflammatory[6], anlagesic[6], estrogenic[7] and antiparkinsonism[8] .The chemistry of heterocyclic composites has been a fascinating field of study for interminability. The conglomerate of novel oxadiazole derivatives and investigation of their chemical and biotic behavior have gained more importance in contemporary decades for biotic, medicinal and agricultural reasons. 1,3,4-Oxadiazoles represent a crucial class of heterocyclic compounds. Their derivatives possess a comprehensive spectrum of biotic activity in both agrochemicals and pharmaceuticals such as insecticidal, herbicidal, antibacterial, antifungal, analgesic, anti-inflammatory, antimalarial, antiviral, anti-HBV, antianexiety, anticancer, anti-HIV, antitubercular and anticonvulsant [9–24].

Quinazolinone nucleus has been getting distinction due to the fact that its derivatives have been found to own wide spectrum of pharmacological properties. Quinazolin-4(3*H*)-one outgrowth are advantageous heterocycles, possessing potent pharmacognosy activities such as antibacterial, antifungal, analgesic, anti-inflammatory, anthelminthic, anticancer, anticonvulsant, antihistaminic, anti-HIV, antiproliferative, antitubercular, antiviral, CNS depressant, cytotoxicity, diuretic and hypolipidemic [25–40].

This investigation was aimed at synthesis and survey of these compounds for their analgesic activity and to acquire more precise information about the course of reaction.

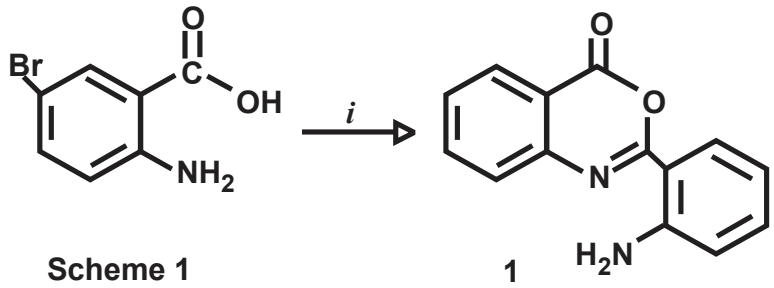
Chemistry.

The presentation of 2-amino substituent is a successful master plan to improve the chemical solidity of benzoxazinone. Due to the microbicidal and pharmacological activities of 4(3H)-quinazolinone derivatives, 2,3-disubstituted derivative of quinazoline-4-one were conglomerated via the interaction of the benzoxazinone derivative with nitrogen nucleophile with the aim of obtaining more accurate information about the course of the reaction and some captivating pharmaceutical compounds. Dissolving 5-bromo anthranillic acid in 100 ml of pyridine in o-amino benzoyl chloride stirring at room temperature for 30 minutes produce the cyclic compound 6-bromo,2-(o-aminophenyl)-3,1-benzoxazin-4(3H)-one(1). The reaction of this compound with 75 mL of hydrazine hydrates for 3 hrs at 120-130^{0}C. the reaction mixture was allowed to cool to room temperature to give 6-bromo-2-(o-aminophenyl)-3-amino-Quinazolin-4(3H)-one **(2).**

Materials and methods

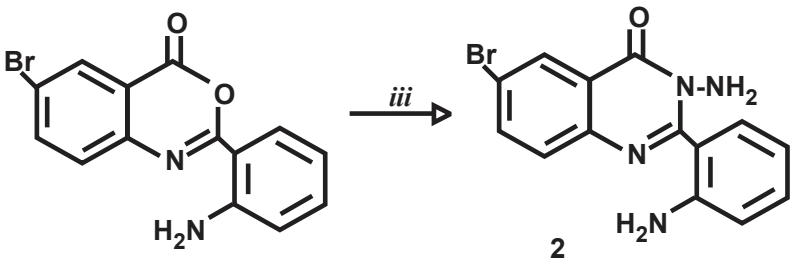
Experimental

All testing agents and cleaners were acquied from sigma-Aldrich, in Germany. Melting points were resolved on a kofler hot stage apparatus and were uncorrected. IR spectra were recorded on a Buck scientific IR M500 instrument. The ^{1}H and ^{13}C NMR spectra were recorded in DMSO-*d*6 at 400 MH_z with HAZ VOLATILE V2. M Chemical shifts Sare reported in ppm relative to tetramethylsilane. Gas chromatography mass spectra were obtained on a Finingan MAT 44S mass spectrophotometer operating at 70eV. Elemental analysis concord favourably with the calculated values. Analytical thin layer chromatography (TLC) was used to praepostor the reactions.



Scheme 1 **1**

***i* = Pyridine/ o-Aminobenzoyl Chloride**



2

Scheme 2

***iii* = $NH_2NH_2H_2O$ / Reflux (3 hours)**

Elemental Analysis

Summary of the structure of the compounds is showned in Table 1. The C and H contents (both theoretically calculated values and actual values) are indicated.

Synthesis of 6-bromo,2-(o-aminophenyl)-3,1-benzoxazin-4(3H)-one(1).

5-bromo anthranillic acid (.16M, 34.72gm) was dissolved in 100 ml of pyridine. To this reaction mixture o-amino benzoyl chloride (.16M, 24.8gm) was added with stirring at room temperature. Stirring continued for 30 mins at the same temperature. This reaction mixture was filtered out and collect the precipitate, which was washed with distilled water and Pet.ether 60/80 to remove the traces of pyridine. The pale creamish crystals obtained were dried at 60^0C. m.p.-190^0C, yield- 75%,

Synthesis of 6-bromo-2-(o-aminophenyl)-3-amino-Quinazolin-4(3H)-one (2).

6-bromo-2-(o-aminophenyl)-3-,1-benzoxazin-4(3H)-one (0.075M, 23.775gm) was refluxed with 75 mL of hydrazine hydrate for 3 hrs at 120-130^0C. the reaction mixture was allowed to cool to room temperature. Pale creamish crystals developed were recrystallized from super dry ethanol. m.p.-178-180^0C, yield-75%,

Pharmacological evaluation

Wistar rats (180-230g) of either sex kept in the laboratory animal house of the Faculty of pharmacy, University of Benin, Benin City, Nigeria were used. The animals were maintained under standard environmental conditions and had free access to standard diet and water. Test compounds were orchestrated orally by gavage in 10% olive oil suspensions at different dose levels). Ethical approval was procued from the Animal Use and Ethics committee of the Faculty of Pharmacy, University of Benin, Benin City, Nigeria.

Results and Discussion

Table 1: Characterization And Physical Data Of Synthesized Compounds

Compound No	Solvent	Formula M. wt	Analysis% Calc/Found	
			C	H
1	Ethanol	$C_{14}H_9BrN_20_2$	42.40	2.27
		(396.8)	42.50	2.28
2	Ethanol	$C_{14}H_9BrN_40$	39.50	2.11
		(424.8)	39.70	2.12

Table 2: ^{13}C-NMR Of Synthesized Compounds

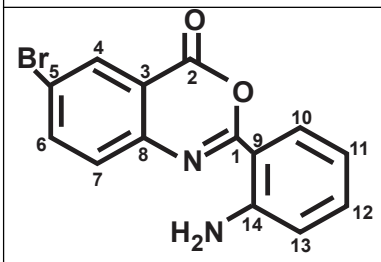
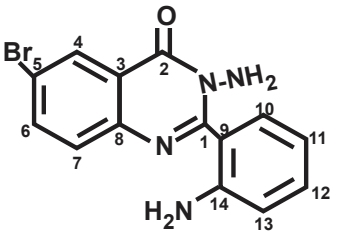
Compound No	δ (ppm) Carbon atom number
 1	157.14(C-1), 160.18(C-2), 121.13(C-3), 127.19(C-4), 112.62(C-5), 112.31(C-6), 121.11 (C-7), 145.06 (C-8), 24.02 (C-9) 112.64(C-10), 112.41(C-11), 112.22 (C-12), 116.07 (C-13), 112.14(C-14).
 2	155.32(C-1), 161.12 (C-2), 121.17(C-3), 127.33 (C-4), 112.11 (C-5), 112.12 (C-6), 122.22 (C-7), 147.14(C – 8), 24.12 (C- 9), 112.51 (C-10), 112.31 (C-11), 121.11 (C-12), 116.09(C – 13), 112.21(C – 14).

Table 3: ^{1}H-NMR Of Synthesized Compounds

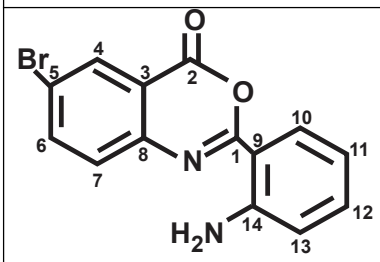
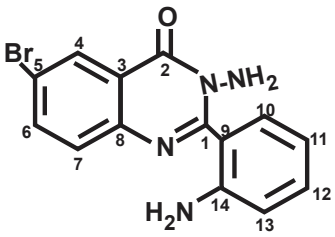
Compound No	δ (ppm)
 1	5.64 (d, 2H of –NH_2), 7.18-7.25 (dd, 1H of-ArH), 7.43-7.86 (m, 5H of –ArH), 6.71 (d, 1H of -ArH).
 2	7.72-7.80 (m, 5H of –ArH), 5.65 (s, 2H of NH_2), 6.18 (s, 2H of –NH_2).

***FIGURE* 1**: Analgesic Activity of Compound 1 and 2 Against Acetic Acid-Induced Writhing **in mice.**

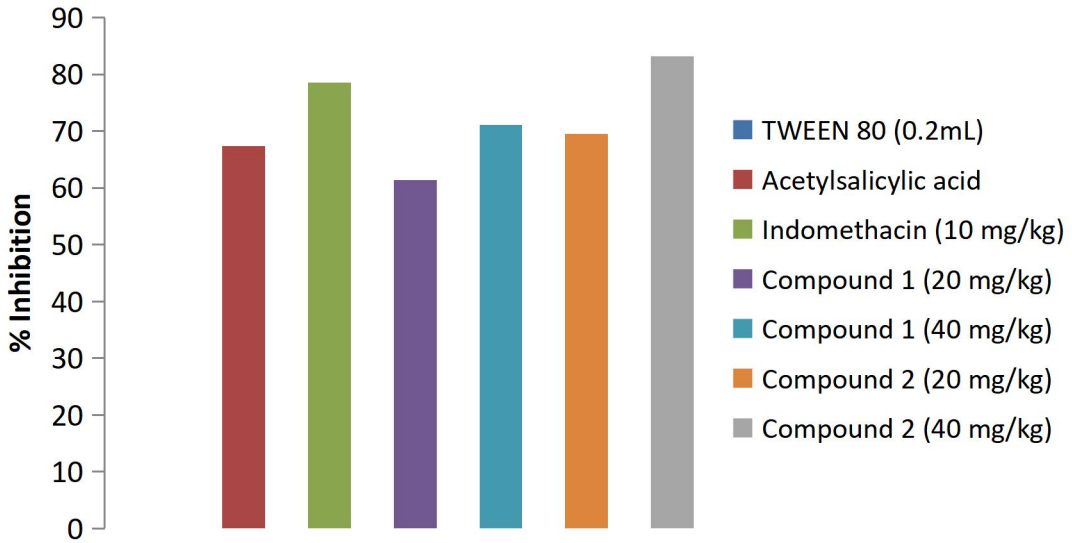


***Figure* 1:** Effects of Test Compounds 1 and 2 on Acetic Acid-Induced Writhing in Mice

***Figure.* 1**: **Compound 1** Acetic acid induce writhing in mice Values are mean ± S.E.M. where number of replicates, n=4 per group, ASP= Aspirin. (*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001)

***FIGURE* 2** : Analgesic Activity of Compound 2 Against Acetic Acid-Induced Writhing **in mice.**

***Figure.* 1**: **Compound 1 and 2** Acetic acid induce writhing in mice Values are mean ± S.E.M. where number of replicates, n=4 per group, ASP= Aspirin. (*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001)

Discussion

The present investigation reported the conglomerate of two outgrowth of quinazolinones, 6-bromo,2-(o-aminophenyl)-3,1-benzoxazin-4(3H)-one(1) and 6-bromo-2-(o-aminophenyl)-3-amino-Quinazolin-4(3H)-one (2) . The compounds were examined for their Analgesic activity. Structural elucidations of compounds synthesized were characterized by correct elemental analysis and careful inspections of spectral data. Looking at the ^{1}H NMR spectra of the compounds synthesized, compound 1 displayed a duplet at δ 5.64 which was due to amino, $–NH_2$ group. Other duplet appeared at δ 7.18 and 7.25 attributed to aromatic protons. Also, ^{1}H NMR spectrum of compound 2 showed a characteristic signal at δ 5.65 and 6.18 (singlet) corresponding to the two amino, $–NH_2$ groups. Two singlets appeared at δ7.41 and 7.10 attributed to aromatic protons. Another signal appeared at 5.80 which is attributed to the protons of the amino group. For the IR spectra, compound 1 were characterized by the presence of 3068 υ C-H str. of the aromatic ring, 1698 cm^{-1} υ C=O str. of the ring, 3365 cm^{-1} 3345 cm^{-1} υ N-H str. of the ring in the region of the compound. Compound 2 was characterized by presence of υ 3048 cm^{-1} υ (C-H str. of the aromatic ring), 3361 cm^{-1} , 3351 cm^{-1} υ (N-H str. of the ring), 1706 cm^{-1} υ (C=O str. of the ring), υ 1316 cm^{-1} region of the compound.

The ^{13}C NMR spectrum of compound 1, revealed signals at δ24.02, attributed to phenyl group, while the aromatic carbon atoms appeared between δ values 112.31 – 160.18 with the carbonyl carbon atom appearing as the highest δ value of 160.18. Similarly, compound 2 showed signals at δ24.12, attributed to phenyl group, while the aromatic carbon atoms appeared between δ values 105.64 - 160.28, with the carbonyl carbon atom appearing as the highest δ value of 160.28.

These compounds synthesized exhibited promising Analgesic activities. The in-vivo analgesic activity of compounds synthesized were determined using carrageenan induced paw edema and the results obtained are summarized in *Figure* 1. Compound 1 has Analgesic activity of 61.33% and 83.18% at 20mg/kg and 40mg/kg dose levels, while Compound 2 has Analgesic activity of 69.49% and 83.18% at 20mg/kg and 40mg/kg dose levels. Compound 2 showed the highest activity at 40mg.kg compared to the other compound 1, and indomethacin a standard Analgesic drug. These compounds synthesized have a higher activity than indomethacin, which is a standard analgesic drug.

Conclusion

The present investigation has showed that the quinazolinone derivatives 1 and 2 have high analgesic activity. Compound 1 has Analgesic activity of 61.33% and 71.14% at 20mg/kg and 40mg/kg dose levels, while Compound 2 has Analgesic activity of 69.49% and 83.18% at 20mg/kg and 40mg/kg dose levels. Compound 2 has a higher Analgesic activity compared to Compound 1 and Indomethacin a standard Analgesic drug. From this result, Compound 2 could be a potential Analgesic and a tool to pharmaceutical drug delivery.

Author declaration

The author hereby declares that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by him.

Ethics approval and consent to participate

Ethic approval, permission to participate and the procedure used was approved by the Ethic approval committee of Ondo State University of Science and Technology, Okitipupa, Ondo State, Nigeria.

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References

[1] Raghavendra N.M., Niranjan M.S., Venkatesh P., Prashantha Kumar B.R., Gowda N.B., Sripathi M.S., Synthesis and biological activity of some substituted 2-phenyl-quinazolin-4-one, Asian Journal of Chemistry, vol.17 no.1, 57-65, 2005.

[2] Mishra P., Namdeo K.P., Jain S.K., Jain S., Synthesis and Antimicrobial Activity of 4-Thiazolidinones, Asian Journal of Chemisry, vol. 11 no.1, 55-58, 1999.

[3] Jatav V., Mishra P., Kashaw S., Stables J.P., Synthesis and CNS depressant activity of some novel 3-[5-substituted-1,3,4-thiadiazole-2-yl]-2-styryl-quinazoline-4(3H)-one, European Journal of Medicinal Chemistry, Vol. XX, 1-7, 2007.

[4] Bhat A.R., Shenoy G., Kotain M., Synthesis and biological activities of Mannich bases of 7-nitro-2-methyl-quinazolin-4(3H)-one, Indian Journal of Heterocyclic Chemistry, vol. 9, 319-320, 2000

[5] Abdel-Hamide S.G., El-Hakim A.E., Abdel-Rahman R.M., Synthesis and biological activities of some new heterocyclic compounds bearing 2-phenyl-6-iodo-quinazolinyl-4-oxy moiety part-1, Indian Journal of Heterocyclic Chemistry, vol. 5, 219-222, 1996.

[6] Maggio B., Daidone G., Demetrio R., Plescia S., Mantione L, Cutuli V.M., Mangano N.G., Caruso A., Synthesis and pharmacological study of ethyl 1-methyl-5-(substituted3,4-dihydro-4-oxoquinazolin-3-yl)-1H-pyrazole-4-acetates, European Journal of Medicinal Chemistry, Vol. 36, 737-742, 2001.

[7] Murugan V., Bhaskaran M.V., Rama Sarma G.V.S., Ramanathan M.,Suresh B., Synthesis and estrogenic screening of some new quinazolinonyl triazoles, Indian Journal of Heterocyclic Chemistry, Vol. 9, 267-270, 2000.

[8] Srivastava V.K., Singh S., Gulati A., Shankar K., Antiparkinsonian agents from Quinazolinylthiazolidinones and Azetidinones, Indian Journal of Chemistry, Vol. 26B, 652-656, 1987.

[9] Zheng X, Li Z, Wang Y, Chen W, Huang Q, Liu C, Song G. Syntheses and insecticidal activities of novel 2,5-disubstituted 1,3,4-oxadiazoles. J Fluorine Chem. 2003;123:163–169. doi:10.1016/S0022-1139(03)00168-4.

[10] Chavan VP, Sonawane SA, Shingare MS, Karale BK. Synthesis, characterization, and biological activities of some 3,5,6-trichloropyridine derivatives. Chem Heterocyclic Compounds. 2006;42:625–630. doi:10.1007/s10593-006-0137-8.

[11] Hollaa BS, Gonsalves R, Shenoy S. Synthesis and antibacterial studies of a new series of 1,2-bis(1,3,4-oxadiazol-2-yl)ethanes and 1,2-bis(4-amino-1,2,4-triazol-3-yl)ethanes. Eur J Med Chem. 2000;35:267–271. doi:10.1016/S0223-5234(00)00154-9.

[12] Liu F, Luo X, Song B, Bhadury PS, Yang S, Jin L, Xue W, Hu D. Synthesis and antifungal activity of novel sulfoxide derivatives containing trimethoxyphenyl substituted 1,3,4-thiadiazole and 1,3,4-oxadiazole moiety. Bioorg Med Chem. 2008;16:3632–3640. doi:10.1016/j.bmc.2008.02.006.

[13] Narayana B, Raj KKV, Ashalatha BV, Kumari NS. Synthesis of some new 2-(6-methoxy-2-naphthyl)-5-aryl-1,3,4-oxadiazoles as possible non-steroidal anti-inflammatory and analgesic agents. Arch Pharm. 2005;338:373–377. doi:10.1002/ardp.200500974.

[14] Koksal M, Bilge SS, Bozkurt A, Sahin ZS, Isik S, Erol DD. Synthesis, characterization and anti-inflammatory activity of new 5-(3,4-dichlorophenyl)-2-(aroyl methyl)thio-1,3,4-oxadiaxoles. Arzneimittel-Forschung. 2008;58:510–514.

[15] Zareef M, Iqbal R, Dominguez NG, Rodrigues J, Zaidi JH, Arfan M, Supuran CT. Synthesis and antimalarial activity of novel chiral and achiral benzenesulfonamides bearing 1,3,4-oxadiazole moieties. J Enz Inhib Med Chem. 2007;22:301–308. doi:10.1080/14756360601114569.

[16] Farghaly AR, El-Kashef H. Synthesis of some new azoles with antiviral potential1. Arkivoc. 2006;11:76–90.

[17] El-Essawy FA, Khattab AF, Abdel-Rahman AAH. Synthesis of 1,2,4-triazol-3-ylmethyl-, 1,3,4-oxa-, and -thiadiazol-2-ylmethyl-1H-[1,2,3]-triazolo[4,5-d]pyrimidinediones. Monatsh Chem. 2007;138:777–785. doi:10.1007/s00706-007-0649-7.

[18] Amr AEE, Mohamed SF, Abdel-Hafez NA, Abdalla MM. Antianexiety activity of pyridine derivatives synthesized from 2-chloro-6-hydrazino-isonicotinic acid hydrazide. Monatsh Chem. 2008;139:1491–1498. doi:10.1007/s00706-008-0949-6.

[19] Kumar A, D'Souza SS, Gaonkar SL, Rai KML, Salimath BP. Growth inhibition and induction of apoptosis in MCF-7 breast cancer cells by a new series of substituted-1,3,4-oxadiazole derivatives. Invest New Drugs. 2008;26:425–435. doi:10.1007/s10637-008-9116-5.

[20] Zareef M, Iqbal R, Al-Masoudi NA, Zaidi JH, Arfan M, Shahzad SA. Synthesis, anti–HIV, and antifungal activity of new benzensulfonamides bearing the 2,5-disubstituted-1,3,4-oxadiazole moiety. Phosphorus Sulfur and Silicon. 2007;182:281–298. doi:10.1080/10426500600919074.

[21] Macaev F, Rusu G, Pogrebnoi S, Gudima A, Stingaci E, Vlad L, Shvets N, Kandemirli F, Dimogloa A, Reynolds R. Synthesis of novel 5-aryl-2-thio-1,3,4-oxadiazoles and the study of their structure-anti-mycobacterial activities. Bioorg Med Chem. 2005;13:4842–4850. doi:10.1016/j.bmc.2005.05.011.

[22] Zarghi A, Tabatabai SA, Faizi M, Ahadian A, Navabi P, Zanganeh V, Shafiee A. Synthesis and anticonvulsant activity of new 2-substituted-5-(2-benzyloxyphenyl)-1,3,4-oxadiazoles. Bioorg Med Chem Lett. 2005;15:1863–1865. doi:10.1016/j.bmcl.2005.02.014.

[23] Alafeefy AM. Synthesis and antimicrobial activity of some new quinazolin-4(3H)-one derivatives. Pharm Biol. 2008;46:751–756. doi:10.1080/13880200802315907.

[24] Sen Gupta AK, Misra HK. Synthesis and evaluation of substituted quinazolone derivatives for antibacterial, antifungal, and antiacetylcholinesterase activities. J Pharm Sci. 1980;69:1313–1317. doi:10.1002/jps.2600691120.

[25] Alagarsamy V, Murugesan S, Sheorey RV. Synthesis and pharmacological investigation of novel 3-(benzyl)-2-substituted amino-3H-quinazolin-4-ones as analgesic and anti-inflammatory agents. Med Chem Res. 2008;17:564–577. doi:10.1007/s00044-008-9098-z.

[26] Jessy EM, Sambanthan AT, Alex J, Sridevi CH, Srinivasan KK. Synthesis and biological evaluation of some novel quinazolones. Indian J Pharm Sci. 2007;69:476–478.

[27] Shukla JS, Agarwal K, Rastogi R. Synthesis of some new 2-substituted 3-[4-(N-arylsulphonylbiguanido)phenyl]quinazolin-4-one hydrochlorides as potential anthelminthic agents. Arch Pharm. 1983;316:525–529. doi:10.1002/ardp.19833160610.

[28] Khalil AA, Abdel Hamide SG, Al-Obaid AM, El-Subbagh HI. Substituted quinazolines, part 2. synthesis and in vitro anticancer evaluation of new 2-substituted mercapto-3H-quinazoline analogs. Arch Pharm. 2003;336:95–103. doi:0365-6233/02/0095.

[29] Laddha SS, Bhatnagar SP. Rapid microwave-assisted solution phase synthesis of 6,8-disubstituted 2-phenyl-3-(substitutedbenzothiazol-2-yl)-4-[3H]-quinazolinones as novel anticonvulsants. Phosphorus Sulfur and Silicon. 2008;183:2262–2273. doi:10.1080/10426500801957766.

[30] Alagarsamy V, Prabakaran L, Murugan RD, Gurumurth G, Bindu P, Arunkumar M, Bothiraja C. Synthesis and antihistaminic activity of some novel 2-mercapto-3-(substitutedmethylamino)quinazolin-4(3H)-ones. Acta Pharm Turcica. 2000;42:33–38.

[31] Alagarsamy V, Murugesan S, Dhanabal K, Murugan M, Clercq E. Anti-HIV, antibacterial and antifungal activities of some novel 2-methyl-3-(substituted methylamino)-(3H)-quinazolin-4-ones. Indian J Pharm Sci. 2007;69:304–307.

[32] Raffa D, Daidone G, Maggio B, Schillaci D, Plescia F. Synthesis and antiproliferative activity of novel 3-(indazol-3-yl)-quinazolin-4(3H)-one and 3-(indazol-3-yl)-benzotriazin-4(3H)-one derivatives. Arch Pharm. 1999;332:317–320. doi:10.1002/(SICI)1521-4184(19999)332:9<317::AID-ARDP317>3.0.CO;2-R.

[33] Mosaad SM, Mohammed KI, Ahmed MA, Abdel-Hamide SG. Synthesis of certain new 6-iodoquinazolines as potential antitubercular agents. J Applied Sci. 2004;4:302–307.

[34] Selvam P, Babu K, Padamraj R, Persoons L, Clercq E. Synthesis, antiviral and cytotoxic activities of some novel 2-phenyl-3-disubstituted quinazolin-4(3H)-ones. African J Pharm Pharmacol. 2008;2:110–115.

[35] Joshi KC, Singh VK, Mehta DS, Sharma RC, Gupta L. Fluorinated quinazolones iii: synthesis and CNS depressant activity of fluorinated quinazolone derivatives. J Pharm Sci. 1975;64:1428–1430. doi:10.1002/jps.2600640843.

[36] Raffa D, Edler MC, Daidone G, Maggio B, Merickech M, Plescia S, Schillaci D, Bai R, Hamel E. Synthesis, cytotoxicity, and inhibitory effects on tubulin polymerization of a new 3-heterocyclo substituted 2-styrylquinazolinones. Eur J Med Chem. 2004;39:299–304. doi:10.1016/j.ejmech.2003.12.009.

[37] Maarouf AR, El-Bendary ER, Goda FE. Synthesis and evaluation of some novel quinazolinone derivatives as diuretic agents. Arch Pharm. 2004;337:527–532. doi:10.1002/ardp.200400869.

[38] Kurogi Y, Inoue Y, Tsutsumi K, Nakamura S, Nagao K, Yoshitsugu H, Tsuda Y. Synthesis and hypolipidemic activities of novel 2-[4 [(diethoxyphosphoryl)methyl]phenyl]quinazolines and 4(3H)-quinazolinones. J Med Chem. 1996;39:1433–1437. doi:10.1021/jm9506938.

[39] Furniss BS, Hannaford AJ, Smith PWG, Tatchell AR. Vogel's Textbook of Practical Organic Chemistry. 5th ed. New York: Wiley; 1989. p. 692.

[40] Katritzky AR, Vvedensky V, Cai X, Rogovoy B, Steel PJ. Syntheses of 5-(2-arylazenyl)-1,2,4-triazoles and 2-amino-5-aryl-1,3,4-oxadiazoles. Arkivoc. 2002;6:82–90.