International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 24s, 2025
https://www.theaspd.com/ijes.php

Design, Synthesis, And Pharmacological Evaluation Of 7-Nitro-2-(4-Nitrophenyl)-3-Substituted Phenylquinazoline-4(3H)-One Derivatives As Potential Anti-Inflammatory Agents

Dr. Akhil Shaikh[1*], Sumerabegum Sayyed[1], Bidrale Supriya Madhav[1], Shaikh Bilal SS[2]., Dr. R.D Ingole[2], Keskar Mohan Sambhaji[2] , Gonge Omkar Aabasaheb[3], Pitale Yogesh Raghunath[2]
[1]Balwantrao Chavan College Of Pharmacy, Naigaon
[2]DJPS College Of Pharmacy Pathri
[3]Shri Ramkrishna Paramhans College of Pharmacy, Hasnapur

Abstract:
The current work was devoted to the production of 7-nitro-2- (4- nitrophenyl)-3-substituted phenylquinazol- 4(3H)- one derivatives and their anti-inflammatory properties assessment. FTIR, mass spectrometry and ^1H NMR were used to characterize the synthesized compounds thoroughly, confirming the structural integrity of the compounds. To determine the anti-inflammatory effects, in-vitro and in-vivo models were conducted namely; egg albumin denaturation assay, carrageenan-induced paw edema and cotton pellet granuloma tests. It was found that all compounds synthesized possessed considerable anti-inflammatory activity, with compounds S1 and S3 proving to show the most promising activities. S1 was among these, demonstrating a potent anti-inflammatory effect, in addition to a high potential in breast cancer. Additionally, there is an early indication that these derivatives can be structurally modified to increase their therapeutic efficacy especially in brain cancer, and therefore they could be used as leads in future drug development.
Keywords: *Anti-inflammatory, quinazolone derivatives, FTIR characterization, in-vivo assays, drug development.*

INTRODUCTION

Inflammation, a fundamental component of the innate immune response, plays a crucial role in host defence and tissue repair.[1] While acute inflammation is typically self-limiting, its dysregulation can lead to chronic inflammation, a recognized contributor to carcinogenesis.[2] Persistent inflammatory responses promote a tumor-supportive microenvironment by inducing genomic instability and mutations. Inflammation-associated cancers may develop through extrinsic pathways triggered by chronic inflammatory conditions or intrinsic pathways involving oncogene activation and tumor suppressor gene suppression.[3]

Key inflammatory mediators such as COX-2, TNF-α, IL-6, NF-κB, and STAT3 have been implicated in tumor progression. Nonsteroidal anti-inflammatory drugs (NSAIDs), particularly aspirin and selective COX-2 inhibitors, have shown promise in reducing the risk and delaying the progression of several cancers, notably colorectal cancer.[4] However, long-term NSAID use is limited by adverse effects, emphasizing the need for safer alternatives.

Quinazolinone derivatives represent a promising class of heterocyclic compounds with a wide range of pharmacological activities including anti-inflammatory and anticancer effects. Structural activity relationship (SAR) studies indicate that substitutions at the 2nd and 3rd positions of the quinazolinone ring significantly enhance biological activity.[5] Considering the interlinked pathways of inflammation and cancer, the present study focuses on the design, synthesis, and evaluation of novel quinazolinone derivatives for their potential dual anti-inflammatory and anticancer activity.[6]

MATERIALS AND METHODS

Chemicals and Reagents

All reagents and solvents were of analytical grade and procured from Himedia, SD Fine Chemicals, Merck, Spectrochem, Alfa Aesar, and SDFCL. Carrageenan, diclofenac sodium, sodium CMC, and NaCl were obtained from New Neeta Chemicals (Pune, India). Chemicals were purified as required using standard procedures.

Instrumentation

- Melting Point: DBK Programmed Melting Point Apparatus (Wasegati Lab Equipment Pvt. Ltd., Mumbai)
- FTIR Spectroscopy: Shimadzu FTIR-AFFINITY-1
- 1H-NMR Spectroscopy: BRUKER AVANCE II 400 MHz
- Mass Spectrometry: Micromass Q-TOF LC-MS
- UV-Vis Spectroscopy: Shimadzu UV Spectrophotometer
- Plethysmometer: LE-7500 (Panlab, Italy)

Synthesis of Quinazolin-4(3H)-one Derivatives

Step I: A solution of 4-chloro/4-nitro anthranilic acid (1 mmol) and trimethylamine (1 mmol) in chloroform (50 mL) was prepared. To this, 2-methoxybenzoyl chloride (1 mmol) was added and stirred at room temperature for 2 h. Subsequently, cyanuric chloride (1 mmol) dissolved in DMF was added and stirred for an additional 4 h. The reaction mixture was washed with ice-cold water, filtered, and the crude product was isolated.

Step II: The intermediate was treated with substituted aniline (1 mmol), glacial acetic acid (20 mL), and sodium acetate (0.25 mg). The reaction mixture was refluxed at 60–70°C for 3–4 h and monitored by TLC. The crude product was purified by recrystallization in ethanol and confirmed by melting point, IR, ^{1}H NMR, and mass spectroscopy.

Structural Characterization

- TLC: Performed using Merck TLC plates (silica gel 60 F254); solvent system: petroleum ether:ethyl acetate (2:3 or 1:4). Spots were visualized under UV light or iodine vapors; Rf values were calculated.
- IR Spectroscopy: Conducted using KBr discs on Shimadzu FTIR-AFFINITY-1; data reported in cm^{-1}.
- Mass Spectrometry: Performed using Micromass Q-TOF LC-MS for molecular weight confirmation and fragmentation patterns.
- ^{1}H-NMR: Spectra were recorded in DMSO using TMS as the internal standard.

PASS Prediction

Prediction of Activity Spectra for Substances (PASS) software was used to estimate the biological activity profiles of synthesized molecules based on structure-activity relationships. Parameters such as Pa (probability to be active), Pi (probability to be inactive), and IEP (Invariant Error of Prediction) were calculated using leave-one-out cross-validation.[7]

In Vitro Anti-inflammatory Assay

Egg Albumin Denaturation Method:

Reaction mixtures containing egg albumin, phosphate buffer (pH 6.4), and test compounds (50–250 µg/mL) were incubated at 37°C for 15 min, then heated at 70°C for 5 min. Absorbance was measured at 660 nm. Diclofenac sodium was used as standard.

$$\% \text{ Inhibition} = 100 \times [At / Ac - 1],$$

where At = absorbance of test sample and Ac = absorbance of control.

In Vivo Anti-inflammatory Activity

Carrageenan-Induced Paw Edema:'Wistar rats (150–250 g) were divided into 12 groups (n=6). Paw edema was induced by subplantar injection of 0.1 mL of 1% carrageenan. Test compounds (5, 10, 20 mg/kg), diclofenac (20 mg/kg), or vehicle (1% CMC) were administered orally 1 h prior to carrageenan injection. Paw volume was measured at 0, 0.5, 1, 2, 3, 4, 5, and 24 h using a plethysmometer.[8]

% Inhibition = [(Positive Control – Test) / Positive Control] × 100

Cotton Pellet-Induced Granuloma:'Sterile cotton pellets (100 ± 1 mg) were implanted subcutaneously in anesthetized rats. Test compounds (10, 20 mg/kg) and standard drug (diclofenac, 10 mg/kg) were administered orally for 7 days. On day 8, pellets were removed, dried, and weighed.[9]

$$\% \text{ Inhibition} = (1 - Wt/Wc) \times 100,$$

where Wt = test group pellet weight and Wc = control group pellet weight.

Statistical Analysis

All data are expressed as mean ± SEM (n=6). Statistical significance was evaluated using one-way ANOVA followed by Dunnett's test using GraphPad INSTAT. Significance was defined as $p<0.05$ (), $p<0.01$ (), and $p<0.001$).

RESULTS

Physicochemical parameter

The Physicochemical parameter of the synthesized test compounds were represented in table

Table 1: Physicochemical parameter of the synthesized test compounds (S1, S2 and S3)

Comp. No.	Nature	Colour	Solubility	Molecular Formula	Mol. wt. (gm)	R_f value	M.P. (^{0}C)	Yield (%)
1 (S1)	Solid	Orange	DMSO	$C_{21}H_{13}ClN_4O_6$	452.80	0.39	204-206	71
2 (S2)	Solid	Yellow	DMSO	$C_{21}H_{14}N_4O_6$	418.35	0.47	215-217	68
3 (S3)	Solid	Yellow	DMSO	$C_{20}H_{11}N_5O_7$	433.33	0.37	207-209	47

7.2. PASS prediction

We performed the PASS prediction of synthesized derivatives of quinazolinone (S1, S2 and S3) for prediction of various biological activities like anti-inflammatory and anti-cancer activity.

Table 2: PASS prediction of test S1

Compound	Activity	Pa	Pi
S1	Anti-inflammatory	0,327	0,138
	Prostaglandin-A1 DELTA-isomerase inhibitor	0,506	0,024
	Transcription factor STAT3 inhibitor	0,550	0,012
	COX inhibitor	0,575	0,009
	Non-steroidal anti-inflammatory agent	0,277	0,050
	Antineoplastic	0,349	0,126
	Antineoplastic (brain cancer)	0,286	0,032

If the value of Pa is greater than 0.7 the probability of experimental biological and pharmacological activity is high and if Pa value is 0.5<Pa>0.7, less is the pharmacological activity.

Table 3: PASS prediction of test S2

Compound	Activity	Pa	Pi
S2	Antiinflammatory	0,316	0,147
	Non-steroidal antiinflammatory agent	0,356	0,028
	Interleukin 6 antagonist	0,442	0,005
	Transcription factor STAT3 inhibitor	0,590	0,008
	Transcription factor STAT inhibitor	0,555	0,011
	COX inhibitor	0,325	0,012
	Histamine release inhibitor	0,393	0,095
	Antineoplastic	0,320	0,141
	Antineoplastic (breast cancer)	0,191	0,099
	Antineoplastic (brain cancer)	0,274	0,039

If the value of Pa is greater than 0.7 the probability of experimental biological and pharmacological activity is high and if Pa value is 0.5<Pa>0.7, less is the pharmacological activity.

Table 4: PASS prediction of test S3

Compound	Activity	Pa	Pi
S3	Antiinflammatory	0,350	0,122
	Interleukin 6 antagonist	0,497	0,004
	Non-steroidal antiinflammatory agent	0,382	0,024
	Transcription factor STAT inhibitor	0,546	0,013
	COX inhibitor	0,502	0,011
	Histamine release inhibitor	0,475	0,049
	Antineoplastic	0,250	0,185
	Antineoplastic (brain cancer)	0,273	0,039
	Antineoplastic (breast cancer)	0,145	0,142

If the value of Pa is greater than 0.7 the probability of experimental biological and pharmacological activity is high and if Pa value is 0.5<Pa>0.7, less is the pharmacological activity.

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 24s, 2025
https://www.theaspd.com/ijes.php

Pharmacological methods for screening of synthesized compounds

***In-vitro* anti-inflammatory activity**

- **Egg albumin protein denaturation**

Table present the anti-inflammatory activity of synthesized test compounds whereas, test S1 showed more effective inhibition of protein denaturation 28.92% at 250 µg/ml, test S2 (21.48 % inhibition) at concentration of 250 µg/ml and test S3 (25.61 % inhibition) at concentration of 250 µg/ml. All the test compounds revealed significant anti-inflammatory effect against the egg albumin denaturation model. While diclofenac sodium demonstrated 39.66% inhibition of protein denaturation at 250µg/ml which was higher than all compounds.

Table 5 : Effect of test compounds on egg albumin protein denaturatation

Design of treatment	Concentration (µg/ml)	Absorbance Mean ± SEM	% Inhibition
Group-I (Control)	-	1.21± 0.054	_
Group-II (Diclo.)	50	0.90±0.013*	25.61%
	100	0.85± 0.040*	29.75%
	150	0.81± 0.033*	33.05%
	200	0.78±0.080**	35.53%
	250	0.73±0.032**	39.66%
Group-III (S1)	50	0.99± 0.004	18.18%
	100	0.95± 0.009	21.48%
	150	0.90± 0.017*	25.61%
	200	0.88±0.001**	27.27%
	250	0.86±0.008**	28.92%
Group-IV (S2)	50	1.12± 0.014	7.43%
	100	1.09± 0.004	9.91%
	150	1.01± 0.004	16.52%
	200	0.98±0.014*	19.00%
	250	0.95±0.008**	21.48%
Group-IV (S3)	50	1.04±0.019	14.04%
	100	1.00±0.047	17.35%
	150	0.97±0.033*	19.83%
	200	0.94±0.040*	22.31%
	250	0.90±0.016**	25.61%

Values expressed as mean± SEM (n=6). ANOVA followed by Dunnett test, *p<0.05, **p<0.01 vs. control group.

***In- vivo* Anti-inflammatory activity**

- **Carrageenan induced rat paw oedema**

In the carrageenan induced rat paw oedema model of anti-inflammatory activity (acute model), test S1, S2 and S3 showed a significant inhibitory effect of the oedema formation from first hour to the fifth hour. The highest inhibitory effect was found in late phase, that is, after second hour ($P < 0.01$) at doses 10 and 20 mg/kg when compared with positive control group. The standard diclofenac sodium 20 mg/kg shows more significant inhibitory effect as compared to test compounds when standard compared with control group.

Table 6 : Effect of test S1 on carrageenan induced rat paw oedema

Groups	Paw volume (ml)							
	0 hr	½ h	1 h	2 h	3 h	4 h	5 h	24 h
Control	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18
Positive Control	0.31± 0.017	0.35± 0.010	0.40± 0.014	0.48± 0.016	0.50± 0.014	0.51± 0.014	0.53± 0.010	0.25± 0.008

Std. Diclo. (20 mg/kg)	0.30± 0.008	0.27± 0.008*	0.25± 0.016**	0.20± 0.012**	0.26± 0.013**	0.30± 0.014**	0.35± 0.020**	0.23± 0.018
Test S1 (5 mg/kg)	0.28± 0.008	0.33± 0.008	0.37± 0.016	0.35± 0.012	0.34± 0.020	0.40± 0.016	0.45± 0.017	0.27± 0.008
Test S1 (10 mg/kg)	0.29± 0.008	0.32± 0.008	0.35± 0.015	0.33± 0.015*	0.31± 0.020**	0.37± 0.016**	0.41± 0.015*	0.26± 0.008
Test S1 (20 mg/kg)	0.31± 0.008	0.31± 0.013	0.34± 0.023*	0.32± 0.014**	0.30± 0.016**	0.37± 0.017**	0.41± 0.016**	0.27± 0.012

Values are expressed as mean ± SEM. (n=6), ANOVA followed by Dunnett test,*p<0.05, **p<0.01 vs. positive control group.

Table 7: % inhibition of test S1 on carrageenan induced rat paw oedema

Groups	**% Inhibition (%)**					
	½ h	**1 h**	**2 h**	**3 h**	**4 h**	**5 h**
Std. Diclo. (20 mg/kg)	22.85	37.5	**58.33**	48	41.17	33.76
Test S1 (5 mg/kg)	5.71	7.5	27.08	32	21.26	15.09
Test S1 (10 mg/kg)	8.57	12.5	31.25	**38**	27.45	22.64
Test S1 (20 mg/kg)	14.14	17.5	37.5	**46**	31.37	26.41

Table 8. : Effect of test S2 on carrageenan induced rat paw oedema

Groups	**Paw volume (ml)**							
	0 hr	**½ h**	**1 h**	**2 h**	**3 h**	**4 h**	**5 h**	**24 h**
Control	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18
Positive Control	0.29± 0.017	0.35± 0.010	0.40± 0.014	0.48± 0.016	0.50± 0.014	0.51± 0.014	0.53± 0.010	0.25± 0.008
Std. Diclo. (20 mg/kg)	0.30± 0.008	0.27± 0.008*	0.25± 0.016**	0.20± 0.012**	0.26± 0.013**	0.30± 0.014**	0.35± 0.020**	0.23± 0.018
Test S2 (5 mg/kg)	0.31± 0.010	0.34± 0.011	0.38± 0.007	0.39± 0.012	0.37± 0.016	0.45± 0.036	0.50± 0.040	0.29± 0.008
Test S2 (10 mg/kg)	0.31± 0.010	0.34± 0.013	0.37± 0.009	0.36± 0.012*	0.34± 0.016*	0.42± 0.036*	0.47± 0.020*	0.29± 0.008
Test S2 (20 mg/kg)	0.32± 0.010	0.33± 0.011	0.36± 0.007*	0.34± 0.012*	0.32± 0.016**	0.39± 0.036**	0.43± 0.040*	0.30± 0.008

Values are expressed as mean ± SEM. (n=6), ANOVA followed by Dunnett test,*p<0.05, **p<0.01 vs. positive control group.

Table 9 : % inhibition of test S2 on carrageenan induced rat paw oedema

Groups	**% Inhibition (%)**					
	½ h	**1 h**	**2 h**	**3 h**	**4 h**	**5 h**
Std. Diclo. (20 mg/kg)	22.85	37.5	**58.33**	48	41.17	33.76
Test S2 (5 mg/kg)	2.85	5	22.91	26	11.76	5.6

Test S2 (10 mg/kg)	2.85	7.5	25	**30**	19.60	11.32
Test S2 (20 mg/kg)	5.71	10	29.16	**36**	23.52	18.86

Table 10: Effect of test S3 on carrageenan induced rat paw oedema

Groups	**Paw volume (ml)**							
	0 hr	**½ h**	**1 h**	**2 h**	**3 h**	**4 h**	**5 h**	**24 h**
Control	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18
Positive Control	0.31± 0.017	0.35± 0.010	0.40± 0.014	0.48± 0.016	0.50± 0.014	0.51± 0.014	0.53± 0.010	0.25± 0.008
Std. Diclo. (20 mg/kg)	0.30± 0.008	0.27± 0.008*	0.25± 0.016**	0.20± 0.012**	0.26± 0.013**	0.30± 0.014**	0.35± 0.020**	0.23± 0.018
Test S3 (5 mg/kg)	0.31± 0.008	0.34± 0.013	0.375± 0.023	0.36± 0.014	0.357± 0.016	0.43± 0.017	0.48± 0.016	0.28± 0.012
Test S3 (10 mg/kg)	0.31± 0.008	0.33± 0.012	0.36± 0.024	0.34± 0.015*	0.33± 0.016**	0.39± 0.019*	0.45± 0.014*	0.27± 0.012
Test S3 (20 mg/kg)	0.31± 0.008	0.31± 0.013	0.34± 0.023*	0.32± 0.014**	0.30± 0.016**	0.37± 0.017**	0.41± 0.016**	0.27± 0.012

Values are expressed as mean ± SEM. (n=6), ANOVA followed by Dunnett test,*p<0.05, **p<0.01 vs. positive control group.

Table 11: % inhibition of test S3 on carrageenan induced rat paw oedema

Groups	**% Inhibition (%)**					
	½ h	**1 h**	**2 h**	**3 h**	**4 h**	**5 h**
Std. Diclo. (20 mg/kg)	22.85	37.5	**58.33**	48	41.17	33.76
Test S3 (5 mg/kg)	3.45	6.12	25	28.6	15.68	9.43
Test S3 (10 mg/kg)	6.12	10	29.16	**34**	23.52	15.09
Test S3 (20 mg/kg)	11.42	15	33.33	**40**	27.45	22.64

- **Cotton pellet-induced granuloma model**

Table shows the effect of test S1, S2 and S3 on cotton pellet-induced granuloma formation in rat. The results indicate that test S1, S2 and S3 at an oral dose of 10 and 20 mg/kg significantly inhibited transudative weight and granuloma formation, but S1 and S3 20 mg/kg showed more inhibitory effect as compared to S2 20 mg/kg. Diclofenac sodium elicited significant reduction. Both standard and test compounds compared with control.

Table 12: Effect of test S1 on Cotton pellet-induced granuloma

Group	**Dose (mg/kg)**	**Granuloma dry weight (mg)**	**% inhibition**
Control	1 % CMC	65.85 ± 1.578	-
Diclofenac	10	40.01 ± 1.346**	39.25%
Test S1	10	52.44 ± 2.406*	20.36%
Test S1	20	45.92 ± 0.587**	30.26%

Values are expressed as mean ± SEM. (n=6), ANOVA followed by Dunnett test,*p<0.05, **p<0.01 vs. control group.

Table 12 : Effect of test S2 on Cotton pellet-induced granuloma

Group	Dose (mg/kg)	Granuloma dry weight (mg)	% inhibition
Control	1 % CMC	65.85 ± 1.578	-
Diclofenac	10	40.01 ± 1.346**	39.25%
Test S2	10	58.05±0.625*	11.84%
Test S2	20	51.55± 0.846**	21.71%

Values are expressed as mean ± SEM. (n=6), ANOVA followed by Dunnett test,*p<0.05, **p<0.01 vs. control group.

Table 13: Effect of test S3 on Cotton pellet-induced granuloma

Group	Dose (mg/kg)	Granuloma dry weight (mg)	% inhibition
Control	1 % CMC	65.85 ± 1.578	-
Diclofenac	10	40.01 ± 1.346**	39.25%
Test S3	10	55.07 ± 0.901*	16.37%
Test S3	20	49.81 ± 0.054**	24.35%

Values are expressed as mean ± SEM. (n=6), ANOVA followed by Dunnett test,*p<0.05, **p<0.01 vs. control group.

DISCUSSION

The synthesized quinazolinone derivatives (S1, S2, and S3) were evaluated for their anti-inflammatory activity using both in-vitro and in-vivo models.[10]

In the in-vitro study (egg albumin denaturation assay), all three compounds demonstrated dose-dependent inhibition of protein denaturation. Compound S1 showed the highest inhibition (28.92% at 250 μg/mL), followed by S3 (25.61%) and S2 (21.48%). Though lower than the standard (diclofenac sodium, 39.66%), these results support their anti-inflammatory potential.[11]

In the in-vivo models, two standard methods were used:

1. Carrageenan-induced rat paw edema (acute inflammation model): This assesses the biphasic inflammatory response where prostaglandins play a major role in the second phase. All three test compounds exhibited significant, dose-dependent inhibition in this model, with S1 showing the strongest effect, suggesting inhibition of prostaglandin synthesis (COX pathway).[12]
2. Cotton pellet-induced granuloma (chronic inflammation model): All compounds significantly reduced granuloma formation, indicating inhibition of the proliferative phase of inflammation. Again, S1 was the most effective, though less than diclofenac.[13]

Overall, compound S1 consistently demonstrated the highest anti-inflammatory activity in both models, followed by S3 and S2. This suggests their potential action via prostaglandin inhibition and COX pathway modulation, aligning with predictions from PASS software.[15]

CONCLUSION

A series of new 7-nitro-2-(4-nitrophenyl)-3-substituted-phenylquinazoline-4-(3H)-one derivatives (S1, S2 and S3) were synthesized as well as characterized for their structure elucidation and screened for anti-inflammatory (In-vivo and In-vitro) vitro) activities. Among the synthesized compounds S1 and S3 exhibit the significant anti- inflammatory activity were not found to be cytotoxic against U87MG cell line. These synthesized compounds showed the prostaglandin inhibition, COX inhibition, IL-6 antagonist and also other properties. So all test compounds may be used for inflammation.

REFERENCES

1. F. Balkwill, K. A. Charles, A. Mantovani, Smoldering and polarized inflammation in the initiation and promotion of malignant disease, Cancer cell. 7 (2005).
2. A. Mantovani, P. Allavena, A. Sica, F. Balkwill, Cancer related inflammation, Nature. 454 (2008) 436–444.
3. F. R. Balkwilla, A. Mantovani, Cancer-related inflammation: Common themes and therapeutic opportunities, Seminars in Cancer Biology. 22 (2012) 33– 40.
4. Wallace B. Morrison Inflammation and Cancer: A Comparative View J Vet Intern Med 2012;26:18–31
5. H. Lu, W. Ouyang, C. Huang, Inflammation, a key event in cancer development, Mol Cancer Res. 4 (2006) 221-233.

6. C. Becker, M. C. Fantini, C. Schramm. TGF-h suppresses tumor progression in colon cancer by inhibition of IL-6 trans-signaling, Immunity. 21 (2004) 491 – 501.
7. F. Balkwill, Tumor necrosis factor or tumor promoting factor? Cytokine Growth Factor Rev. 13 (2002) 135 – 41.
8. A, Muller, B. Homey, H. Soto, Involvement of chemokine receptors in breast cancer metastasis, Nature. 410 (2001) 50 – 60.
9. K. Heyninck, R. Beyaert, A20 inhibits NF-κB activation by dual ubiquitin editing functions. Trends, Biochem Sci, 30 (2005) 1 – 4.
10. L. J. Hofseth, S. P, Hussain, G. N. Wogan, C. C. Harris, Nitric oxide in cancer and chemoprevention, Free Radic Biol Med. 34 (2003) 955 – 68.
11. C. J. Buskens, B. P. Van Rees, A. Sivula A, Prognostic significance of elevated cyclooxygenase-2 expression in patients with adenocarcinoma of the esophagus, Gastroenterology. 122 (2002) 1800 – 7.
12. Y. Makino, H. Nakamura, E. Ikeda E, Hypoxia-inducible factor regulates survival of antigen receptor-driven T cells, J Immunol. 171 (2003) 6534 – 40.
13. D. R. Hodge, E. M. Hurt, W. L. Farrar, The role of IL-6 and STAT3 in inflammation and cancer, Eur J Cancer. 41 (2005) 2502 – 12.
14. H. Y. Cho, S. P. M. Reddy, M. Yamamoto, S. R, Kleeberger. The transcription factor NRF2 protects pulmonary fibrosis, FASEB J. 18 (2004) 1258 – 60.
15. A. Rao, C. Luo, P. G. Hogan, Transcription factors of the NFAT family: regulation and function, Annu Rev Immunol. 15 (1997) 707 – 47.
16. C. H. Koehne, R. N. Dubois, COX-2 inhibition and colorectal cancer, Semin. Oncol. 31 (2004) 12–21.
17. E. T. Chang, T. Zheng, E. G. Weir, M. Borowitz, R. B. Mann, D. Spiegelman, N. E. Mueller, Aspirin and the risk of Hodgkin's lymphoma in a population-based case-control study, J. Natl. Cancer Inst. 96 (2004) 305–315.
18. K. Garber, Aspirin for cancer chemoprevention: Still a headache? J. Natl. Cancer Inst. 96 (2004) 252–253.
19. E. S. Schernhammer, J. H. Kang, A. T. Chan, D. S. Michaud, H.G. Skinner, E. Giovannucci, G. A. Colditz, C. S. Fuchs, A prospective study of aspirin use and the risk of pancreatic cancer in women. J Natl Cancer Inst. 96 (2004) 2–28.
20. F. Balkwill, A. Mantovani, Inflammation and cancer: back to Virchow? Lancet. 357 (2001) 539–45.
21. S. K. Krishnan, S. Ganguly, R. Veerasamy, B. Jan, Synthesis, antiviral and cytotoxic investigation of 2-phenyl-3-substituted quinazolin-4(3H)-ones, European Review for Medical and Pharmacological Sciences. 15 (2011) 673-681.
22. M. Gnana Ruba Priya, K. Girija, N. Ravichandran, In-vitro study of anti-inflammatory and antioxidant activity of 4-(3h) – quinazolinone derivatives, Rasayan J Chem. 4 (2011) 418-424.
23. V. Jatav, P. Mishra, S. Kashaw, J. P. Stables, CNS depressant and anticonvulsant activities of some novel 3-[5-substituted 1,3,4-thiadiazole-2-yl]-2-styryl quinazoline-4(3H)-ones, European Journal of Medicinal Chemistry. 43 (2008) 1945-1954.
24. M. Chaudhary, P. Chaudhary, Synthesis, characterization and pharmacological evaluations of substituted quinazolin-4-(*3h*)-one derivative as novel anticonvulsant agents, World Journal of Pharmacy and Pharmaceutical Sciences. 3 (2014) 1292-1309.
25. K. Vijayakumar, A. A Jafar, G. Thiruneelakandan, Synthesis, antimicrobial, and anti-HIV1 activity of quinazoline-4(3*h*)-one derivatives, Journal of Applied Chemistry. 2013
26. G. Saravanan, V. Alagarsamy, R. P. Chinnasamy, Synthesis and evaluation of antioxidant activities of novel quinazolinone derivatives, International Journal of Pharmacy and Pharmaceutical Sciences. 2 (4) (2010).
27. S. Rajasekaran, G. K. Rao, N. Sharma, Synthesis and evaluation of biological activity of some 2, 3-substituted quinazolin-4(3h)-ones, RGUHS J Pharm Sci. 3 (2013).
28. Y. S. Birhan, A. A. Bekhit, A. Hymete, In-vivo antimalarial evaluation of some2, 3-disubstituted-4 (3*H*)-quinazolinone derivatives, BMC Res Notes. 8 (2015) 589.
29. D. Kohli, S. R. Hashim, S. Vishal, M, Sharma, A. K. Singh, Synthesis and antibacterial activity of quinazolinone derivatives, International journal of pharmacy and pharmaceutical sciences, 1 (2009)