Acta Pharm. **59** (2009) 355–364
10.2478/v10007-009-0026-7

Short communication

Synthesis of some novel triazole derivatives as anti-nociceptive and anti-inflammatory agents

AIYALU RAJASEKARAN[1]*
KALASALINGAM ANANDA RAJAGOPAL[2]

[1]*KMCH College of Pharmacy Coimbatore, Tamilnadu, India*

[2]*AK College of Pharmacy Krishnankoil, Tamilnadu, India*

Eight novel 1-[2-(1*H*-tetrazol-5-yl)ethyl]-1*H*-benzo[*d*][1,2,3]triazoles (**3a-h**) have been synthesized in order to obtain new compounds with potential anti-nociceptive and anti-inflammatory activity. The titled compounds were synthesized by the condensation of 1-[2-(1*H*-tetrazol-5-yl) ethyl]-1*H*-benzotriazole (**2**) and appropriate acid chlorides. Compound **2** was synthesized by reacting 3-(1*H*--benzo[*d*][1,2,3]triazol-1-yl)propanonitrile (**1**) with sodium azide and ammonium chloride in the presence of dimethylformamide. The synthesized compounds were characterized by spectroscopic methods (IR, ^{1}H NMR, mass spectroscopy) and elemental analysis. The titled compounds were evaluated for anti-nociceptive activity by the hot plate method and the writhing response method, and anti-inflammatory activity was evaluated by the carrageenan induced paw edema method. 5-(2-(1*H*-benzo[*d*][1,2,3]triazo-1-yl)ethyl)-1*H*-tetrazol-1-yl)(4-aminophenyl)methanone (**3d**) and 5-(2-(1*H*-benzo[*d*][1,2,3]triazo-1-yl)ethyl)--1*H*-tetrazol-1-yl)(2-hydroxyphenyl)methanone (**3g**) exhibited significant anti-nociceptive activity. 1-(2-(1-Tosyl--1*H*-tetrazol-5-yl)ethyl)-1*H*-benzo[*d*][1,2,3]triazole (**3c**) and 4,5-(2-(1*H*-benzo[*d*][1,2,3]triazo-1-yl)ethyl)-1*H*-tetrazol-1-yl sulfonyl)benzenamine (**3f**) elicited superior anti-inflammatory activity compared to other synthesized compounds. Further investigations are needed to discern the mechanism of action.

Keywords: synthesis, 1-[2-(1*H*-tetrazol-5-yl)ethyl]-1*H*-benzo[*d*][1,2,3]triazoles, anti-nociception, anti-inflammation

Accepted July 8, 2009

Tetrazole is a five-membered ring structure composed of four nitrogen atoms and one carbon atom and is used as an intermediate in the synthesis of pharmaceuticals, especially cephalosporins. Tetrazole and its derivatives have been reported to possess anti--nociceptive (1), anti-inflammatory (2), antimicrobial (3) and anticonvulsant properties (4, 5). Benzotriazole moiety is a versatile lead molecule in pharmaceutical development

* Correspondence; e-mail: rsekaran2001in@yahoo.co.in

and has a wide range of biological activities, *e.g.*, anti-inflammatory (6), anti-nociceptive (7), anticonvulsant (8), antimicrobial (9), protein kinase inhibiting (10) and immunosuppressive activities (11). Our research was focused on incorporation of the benzotriazole moiety into tetrazoles based upon the hypothesis that this modification would improve efficacy, since both moieties are noted for their anti-nociceptive and anti-inflammatory properties. Thus, a series of novel 1-[2-(1*H*-tetrazol-5-yl)ethyl]-1*H*-benzo[*d*][1,2,3]triazoles were synthesized and tested for their anti-nociceptive and anti-inflammatory properties.

EXPERIMENTAL

Melting points were determined using a melting point apparatus (Veego, VMP III, India) and were not corrected. Infrared spectra were obtained on a Perkin Elmer FTIR spectrophotometer 1600 series (Perkin Elmer, USA) using potassium bromide discs. ^{1}H NMR spectra were recorded on a Bruker 400 MHz spectrophotometer (Bruker, USA). Chemical shifts are reported in parts per million (δ) units relative to an internal standard

Table I. Physical and analytical data of synthesized compounds

Compd.	Mol. formula	Mol. mass[a]	M.p. (°C)	Yield (%)	Elemental analysis (calcd./found, %)		
					C	H	N
1	$C_9H_8N_4$	172.19	89–92	73	62.87 62.62	4.68 4.64	32.54 32.42
2	$C_9H_9N_7$	215.22	68–72	78	50.23 50.39	4.22 4.14	45.56 43.52
3a	$C_{16}H_{13}N_7O$	319.33	95–102	76	60.18 60.34	4.10 4.42	30.70 30.68
3b	$C_{16}H_{12}N_8O_3$	364.32	80–85	76	52.75 52.64	3.32 3.42	30.76 30.58
3c	$C_{16}H_{15}N_7O_2S.$	369.41	180–182	73	52.02 52.34	4.09 4.14	26.54 26.78
3d	$C_{16}H_{14}N_8O$	334.34	220–226	75	57.48 57.34	4.22 4.33	33.52 33.68
3e	$C_{16}H_{14}N_8O$	334.34	140–146	64	57.48 57.34	4.22 4.14	33.52 33.21
3f	$C_{15}H_{14}N_8O_2S$	370.39	242–245	72	48.64 48.49	3.81 3.62	30.25 30.43
3g	$C_{16}H_{13}N_7O_2$	335.32	167–170	67	57.31 57.34	3.91 4.05	29.24 29.28
3h	$C_{16}H_{13}N_7O_2$	335.32	234–237	66	57.31 57.44	3.91 4.08	29.24 29.38

[a] Molecular mass determination by mass spectral analysis (M+)

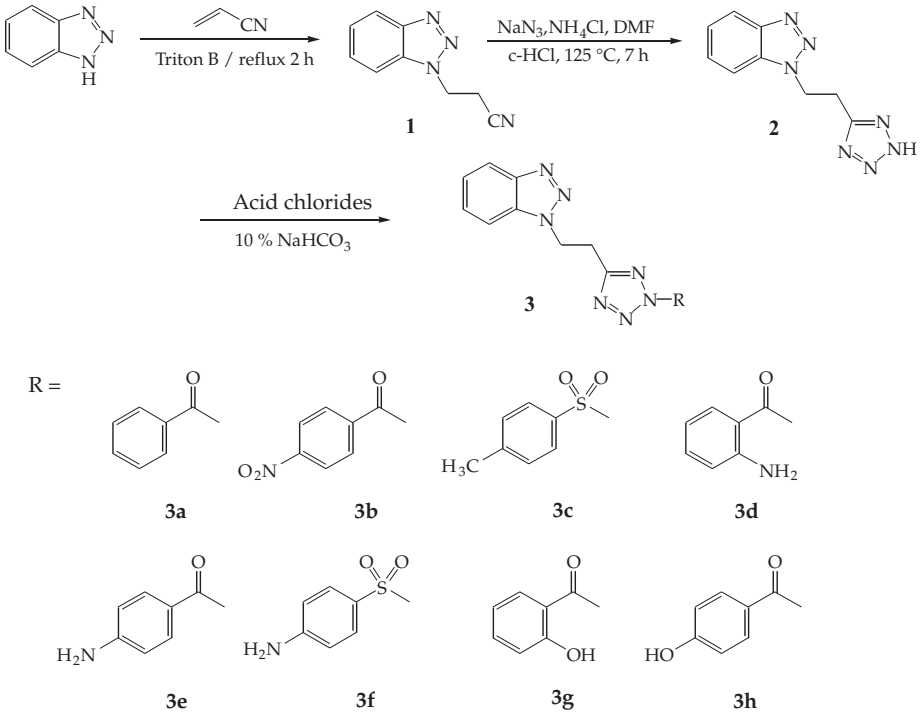
of tetramethylsilane. Mass spectra were recorded on a mass spectrometer (Jeol JMS-DX 303 (Jeol, Japan) and Finnigan MAT 8230 (Finnigan MAT, Germany). Elemental analyses were performed on a Heraeus Carlo Erba 1108 (Elementar, USA) and the analyses were within ± 0.4 % of theoretical values.

*Synthesis of 3-(1*H*-Benzo[*d*][1,2,3]triazol-1-yl)propanonitrile (**1**)*

Benzotriazole (50 mmol) was mixed with acrylonitrile (12.5 mL) and cooled in an ice bath. A resorcinol crystal was added to prevent polymerization. Triton B (2 mL, 40 % *V*/*V*) was added dropwise under shaking and a vigorous reaction was observed. It was allowed to subside and was then refluxed on a steam bath for 2 h. The solution was cooled, extracted with ethylene dichloride and dried over anhydrous sodium sulphate. The dried nitrile was recrystallized from ether. The desired 3-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)propanonitrile (**1**) was obtained as a solid.

Table II. Spectral data of synthesized compounds

Compd.	IR (KBr) (cm^{-1})	^{1}H NMR (DMSO-d_6) (δ, ppm)
1	2958 (C-H), 2254 (C≡N), 1456 (C-H)	2.7 (2H, t, J = 7.1 Hz, CH_2), 4.4 (2H, t, J = 7.1 Hz, CH_2), 6.8–7.3 (8H, m, Ar-H).
2	3462 (N-H), 2926 (C-H), 2853 (C-H), 1639 (C=N), 1458 (C-H), 1286 (N-N=N-), 1197 (tetrazole ring)	2.8 (2H, t, J = 7.1 Hz, CH_2), 4.3 (2H, t, J = 7.1 Hz, CH_2), 6.8–7.3 (8H, m, Ar-H).
3a	2930 (C-H), 1695 (C=O), 1437 (C-H), 1282 (N-N=N-), 1108 and 1138 (tetrazole ring)	2.8 (2H, t, J = 7.1 Hz, CH_2), 4.3 (2H, t, J = 7.1 Hz, CH_2), 6.8–7.3 (9H, m, Ar-H)
3b	2887 (C-H), 1774 (C=O), 1576 (NO_2), 1457 & 1367 (C-H), 1283 (N-N=N-), 1110 (tetrazole ring)	2.8 (2H, t, J = 7.1 Hz, CH_2), 4.3 (2H, t, J = 7.1 Hz, CH_2), 6.8–8.1 (8H, m, Ar-H)
3c	2930 (C-H), 1774 (C=O), 1618 (C=N), 1457 (C-H), 1283 (N-N=N-), 1108, 1133 (tetrazole ring), 1044 (SO_2)	δ 2.1 (3H, s, CH_3), 2.8 (2H, t, J =7.1 Hz, CH_2), 4.3 (2H, t, J = 7.1 Hz, CH_2), 6.8–7.7 (8H, m, Ar-H)
3d	3464 (N-H), 2798 (C-H), 1666 (C=O), 1457 (C-H), 1301 (N-N=N-), 1105 and 1162 (tetrazole ring)	2.8 (2H, t, J = 7.1 Hz, CH_2), 4.3 (2H, t, J = 7.1 Hz, CH_2), 4.5 (2H, s, NH_2), 6.8–7.3 (8H, m, Ar-H)
3e	3463 (N-H), 2798 (C-H), 1666 (C=O), 1486 (C-H), 1301 (N-N=N-), 1105 and 1162 (tetrazole ring)	2.8 (2H, t, J = 7.1 Hz, CH_2), 4.3 (2H, t, J = 7.1 Hz, CH_2), 4.5 (2H, s, NH_2), 6.8–7.7 (8H, m, Ar-H)
3f	3383 (N-H), 1434 (CH), 1282 (N-N=N), 1132 (tetrazole ring), 1031(SO2)	2.8 (2H, t, J = 7.1 Hz, CH_2), 4.3 (2H, t, J = 7.1 Hz, CH_2), 4.5 (2H, s, NH_2), 6.8–7.3 (8H, m, Ar-H)
3g	3372 (O-H), 1774 (C=O), 1457 (C-H), 1295 (N-N=N-), 1138 (tetrazole ring	2.1 (3H, s, CH_3), 2.8 (2H, t, J = 7.1 Hz, CH_2), 4.3 (2H, t, J = 7.1 Hz, CH_2), 5 (1H, s, OH), 6.8–7.6 (8H, m, Ar-H)
3h	3371 (O-H), 1744 (C=O), 1458 (C-H), 1283 (N-N=N-), 1108 and 1138 (tetrazole ring)	2.1 (3H, s, CH_3), 2.8 (2H, t, J = 7.1 Hz, CH_2), 4.3 (2H, t, J = 7.1 Hz, CH_2), 5 (1H, s, OH), 6.8–7.9 (8H, m, Ar-H)



Scheme 1

*Synthesis of 1-[2-(1*H*-tetrazol-5-yl)-ethyl]-1*H*-benzotriazole (***2***)*

Equimolar quantities of compound (**1**), sodium azide, dimethylformamide (10 mL) and ammonium chloride were heated in an oil bath for 7 h at 125 °C. The solvent was removed under reduced pressure, the residue was dissolved in 100 mL of water and carefully acidified with concentrated hydrochloric acid to pH 2. The solution was cooled to 5 °C in an ice bath. Compound **2** was recrystallized from aqueous methanol.

*Synthesis of 1-[2-(1*H*-tetrazol-5-yl)ethyl]-1*H*-benzo[*d*][1,2,3]triazoles (**3a-h**). General procedure*

Compound **2** was treated with an equimolar amount of aromatic acid chlorides in 10 mL of sodium bicarbonate solution (10 % *m*/*V*). The mixture was shaken vigorously until the odor of aromatic acid chloride disappeared. The solids which separated out were filtered and dried. Recrystallization of the dried compounds from aqueous ethanol yielded compounds **3a-h**.

Pharmacological screening

Acute toxicity study. – This involves estimation of the median lethal dose (LD_{50}) (12), which is the dose that will kill 50 % of the animal population within 24 h post treatment with the test substance. All animal experiments were conducted under the conditions of the Animal Scientific Procedures. The experimental protocol was approved by the Animal Care Review Committee of the AK College of Pharmacy, India. Groups of Swiss albino mice consisted of six animals and were maintained in colony cages at 25 ± 2 °C, relative humidity of 45–55 %, under a 12 h light and dark cycle; they were fed standard animal feed and water *ad libitum*. They were treated intraperitoneally with different doses of test compounds (200, 400, 600, 800, 1000 mg kg^{-1}). The animals were then observed for 24 h for any behavioral effects such as nervousness, excitement, dullness, in-coordination or even death. The LD_{50} was found to be 180 mg kg^{-1}.

Hot plate method. – All the newly synthesized compounds were tested for anti-nociceptive activity by the Eddy and Leimbach method (13). Swiss albino mice were divided into ten groups of six mice each. One group served as control and was administered 0.5 % (*V*/*V*) Tween 80 (0.5 mL) suspension. One group was administered the standard drug pentazocine (Sigma, USA) intraperitoneally at a dose of 5 mg kg^{-1} 15 minutes before the analgesic activity evaluation. Tween 80 suspension (0.5 %, *V*/*V*) of test compounds **3a-h** was administered intraperitoneally at a dose at 18 mg kg^{-1} to the remaining groups 15 minutes before the analgesic activity evaluation. The reaction time in seconds was noted for all the groups on Eddy's hot plates before and 15 minutes after administration of test compounds and pentazocine (Table III).

Table III. Evaluation of anti-nociceptive activity by the hot plate method

Compd. (dose)	Reaction time (s)	
	before treatment[a]	after 15 minutes[a]
3a (18 mg kg^{-1})	3.75 ± 0.55	8.66 ± 0.37[b]
3b (18 mg kg^{-1})	3.66 ± 0.66	7.33 ± 0.42[c]
3c (18 mg kg^{-1})	4.24 ± 0.89	12.33 ± 0.55[b]
3d (18 mg kg^{-1})	3.88 ± 0.56	13.00 ± 0.34[b]
3e (18 mg kg^{-1})	4.52 ± 0.76	9.50 ± 0.43[b]
3f (18 mg kg^{-1})	3.98 ± 0.24	10.68 ± 0.88[b]
3g (18 mg kg^{-1})	2.98 ± 0.35	13.83 ± 0.34[b]
3h (18 mg kg^{-1})	4.12 ± 0.55	11.50 ± 0.42[b]
Control	3.32 ± 0.46	3.33 ± 0.55
Pentazocine (5 mg kg^{-1})	4.68 ± 0.29	13.34 ± 0.46[b]

Control – no synthesized compound and paracetamol.
[a] Mean ± SEM (n = 6).
Significant difference compared with the control: [b] $p < 0.001$, [c] $p < 0.01$.

Acetic acid induced writhing method. – The synthesized compounds were also tested for anti-nociceptive activity by the acetic acid induced writhing method (14). The animals were divided into ten groups of six. The control group of animals was administered 0.5 % (*V*/*V*) Tween 80 (0.5 mL) suspension. The standard drug paracetamol (Micro Labs, India) was administered intraperitoneally at a dose of 2.5 mg kg^{-1}. Tween 80 suspension (0.5 %, *V*/*V*) of test compounds were administered intraperitoneally at a dose of 18 mg kg^{-1}. Twenty minutes after administration of the test compounds and a standard, all groups of mice were given the writhing agent, 3 % (*V*/*V*) aqueous acetic acid at a dose of 2 mL kg^{-1} intraperitoneally. The total number of writhings produced in these animals was counted visually for 15 minutes and the number of writhings produced in treated groups was compared with that in the control group. The results given in Table IV are expressed as percentage protection.

Anti-inflammatory activity. – The anti-inflammatory activity was evaluated by the carragenean induced paw edema method (15). Albino rats of Wistar strain, weighing 100–200 g, of either sex were divided into ten groups of six animals each. The animals were maintained under normal environmental conditions. They were fed standard feed and water *ad libitum*. Tween 80 suspension (0.5 %, *V*/*V*) of test compounds was administered intraperitoneally at a dose of 18 mg kg^{-1}. The control group was given only 0.5 % (*V*/*V*) Tween 80 (0.5 mL) suspension. One group was administered diclofenac sodium as standard, intraperitoneally at a dose of 2 mg kg^{-1}. Thirty minutes after the administration of test compounds and diclofenac sodium, paw edema was induced in albino rats by injecting 0.1 mL of carragenean suspension (1 %, *V*/*V* in normal saline), into subplantar region of the left hind paw of each rat. Tree hours after carragenean injection, the increase in paw volume was measured with a plethysmometer. The anti-inflammatory activity was measured in terms of percentage inhibition of edema and analyzed (Table V).

Table IV. Anti-nociceptive activity by the acetic acid-induced writhing method

Compd. (dose)	No. of writhings (after 15 minutes)[a]	Protection (%)
3a (18 mg kg^{-1})	28 ± 1[b]	58
3b (18 mg kg^{-1})	34 ± 1	37
3c (18 mg kg^{-1})	23 ± 0[b]	62
3d (18 mg kg^{-1})	16 ± 1[b]	70
3e (18 mg kg^{-1})	19 ± 1[b]	67
3f (18 mg kg^{-1})	21 ± 1[b]	63
3g (18 mg kg^{-1})	9 ± 1[b]	85
3h (18 mg kg^{-1})	14 ± 1[b]	72
Control	54 ± 1	–
Paracetamol (2.5 mg kg^{-1})	9 ± 1[b]	88

Control – no synthesized compound and diclofenac sodium.
[a] Mean ± SEM (n = 6).
Significant difference compared with the control: [b] $p < 0.001$, [c] $p < 0.01$.

Table V. Anti-inflammatory activity of synthesized compounds by the carragenean-induced paw edema method

Compd. (dose)	Paw volume (in mL)[a]	Inhibition after 3 h (%)
3a (18 μg kg^{-1})	0.38 ± 0.02	14
3b (18 μg kg^{-1})	0.39 ± 0.03	11
3c (18 μg kg^{-1})	0.24 ± 0.04	45[b]
3d (18 μg kg^{-1})	0.36 ± 0.03	18
3e (18 μg kg^{-1})	0.38 ± 0.02	14
3f (18 μg kg^{-1})	0.23 ± 0.03	47[b]
3g (18 μg kg^{-1})	0.30 ± 0.22	32
3h (18 μg kg^{-1})	0.31 ± 0.32	30
Control	0.44 ± 0.19	–
Diclofenac sodium (2 μg kg^{-1})	0.17 ± 0.02	61[b]

Control – no synthesized compound and diclofenac sodium.
[a] Mean ± SEM (n = 6).
Significant difference compared with the control: [b] $p < 0.01$.

Statistical analysis

Statistical analysis of the biological activity of synthesized compounds on animals was evaluated using a one-way analysis of variance (ANOVA). In all cases, *posthoc* comparisons of the means of individual groups were performed using Tukey's test. All values were expressed as mean ± SEM. The GraphPad Prism 3.0 version was used for statistical analysis.

RESULTS AND DISCUSSION

The key intermediate 3-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)propanonitrile (**1**) was prepared by refluxing 1*H*-benzo[*d*][1,2,3]triazole with acrylonitrile and Triton B. IR spectra of compound **1** showed intense peaks at 2254 cm^{-1} and confirmed the formation of nitrile (CN). Two triplets at δ 2.7 and 4.4 ppm of ^{1}H NMR spectrum confirmed the presence of two methylene protons and a multiplet between δ 6.8 and 7.3 ppm confirmed the presence of aromatic protons (8H) in compound **1.** Further, the molecular ion recorded (m/z 172 [M+]) in the mass spectrum is also in agreement with the molecular mass of the compound.

1-[2-(1*H*-tetrazol-5-yl)ethyl]-1*H*-benzotriazole (**2**) was synthesized by reacting 3-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)propanonitrile (**1)** with sodium azide and ammonium chloride in the presence of dimethylformamide. The IR spectrum of compound **2** showed disappearance of CN stretching signals of nitrile. It showed a peak for the tetrazole ring at 1197 cm^{-1}, –N–N=N– stretching at 1286 cm^{-1} and NH stretching at 3462 cm^{-1}. The ^{1}H NMR spectrum of compound **2** showed two triplets for methylene protons and a

multiplet at δ 6.8–7.3 ppm for aromatic (8H) protons. Molecular ion recorded in the mass spectrum (m/z 215 [M+]) confirmed the assigned structure.

1-[2-(1*H*-tetrazol-5-yl)ethyl]-1*H*-benzotriazole (**2**) has a free secondary amino group which can readily react with acid chlorides. Hence, the titled compounds, 1-[2-(1*H*-tetrazol-5-yl)ethyl]-1*H*-benzo[*d*][1,2,3]triazoles (**3a-h**), were obtained by substitution of various aromatic carbonyl and sulphoxide moieties using aromatic acid chlorides in the presence of sodium bicarbonate solution. Formation of the titled compounds was confirmed by the disappearance of the peak due to NH stretching of compound **2**. IR spectra of all compounds **3a-h** showed the presence of peaks due to (N-N=N) and the tetrazole ring. ^{1}H NMR spectra of all compounds **3a-h** showed absorption signals at δ 2.8 and 4.3 ppm for the two methylene protons and multiplet signals between 6.8 and 7.8 ppm for the presence of aromatic protons. Mass spectra of the titled compounds showed molecular ion peaks corresponding to their molecular formula. Elemental analysis satisfactorily confirmed the elemental composition and purity of the synthesized compounds.

The results of analgesic testing indicated that the test compounds **3d** and **3g** exhibited significant analgesic activity after 15 min of reaction time (13 and 13.83), tested by the hot plate method. Substitution of the amino group in **3d** and hydroxyl group in **3g** in *ortho* position of aryl moiety increased the anti-nociceptive activity. All other compounds exhibited moderate anti-nociceptive activity. With the exception of **3b**, all the compounds exhibited anti-nociceptive activity tested by the acetic acid induced writhing method at a dose of 18 mg kg^{-1}. The anti-nociceptive activity of compounds **3d**, **3e**, **3g** and **3h** was found to be superior compared to other synthesized compounds. Compounds **3d** and **3g** were found to be the most active derivatives tested by both the hot plate method and the acetic acid induced writhing method; they possess 2-aminobenzoyl and 2-hydroxybenzoyl group at the tetrazole moiety of the benztriazole framework.

Synthesized compounds **3a-h** exhibited poor anti-inflammatory activity (16–22 % protection only) against carragenean induced paw edema, whereas the standard drug diclofenac sodium (Novartis Laboratories, India) showed 61 % inhibition under similar conditions. Among the compounds tested, compounds **3c** and **3f** exhibited mild anti-inflammatory activity. Inclusion of substituted benzoyl moiety in the tetrazole moiety of benzotriazole framework did not produce any marked inhibition of edema. However, inclusion of substituted sulfonyl moiety in **3f** resulted in mild anti-inflammatory properties.

CONCLUSIONS

In the present study, synthesis of a new series of 1-[2-(1*H*-tetrazol-5-yl)ethyl]-1*H*--benzo[*d*][1,2,3]triazoles (**3a-h**) has been described. Compounds **3d** and **3g** were found to be the most active derivatives with promising anti-nociceptive activity. We can deduce from the results that replacement of active hydrogen from the tetrazole moiety with substituted benzoyl and sulfonyl moiety can create potent anti-nociceptive compounds, whereas replacement of active hydrogen from the tetrazole moiety with substituted sulfonyl moiety may lead to mild anti-inflammatory activity. Further studies on structural modifications are needed to increase the anti-inflammatory activity.

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S A Ž E T A K

Sinteza novih derivata triazola kao anti-nociceptivnih i protuuaplnih agenasa

AIYALU RAJASEKARAN i KALASALINGAM ANANDA RAJAGOPAL

Sintetizirano je osam novih 1-[2-(1*H*-tetrazol-5-il)etil]-1*H*-benzo[*d*][1,2,3]triazola (**3a-h**) s potencijalnim anti-nociceptivnim i protuupalnim djelovanjem. Navedeni spojevi pripravljeni su kondenzacijom 1-[2-(1*H*-tetrazol-5-il)etil]-1*H*-benzotriazola (**2**) i odgovarajućih kiselinskih klorida. Spoj **2** dobiven je reakcijom 3-(1*H*-benzo[*d*][1,2,3]triazol-1-il)propanonitrila (**1**) s natrijevim azidom i amonijevim kloridom u prisutnosti dimetilformamida. Sintetizirani spojevi su karakterizirani spektroskopskim metodama (IR, ^{1}H NMR, spek-

troskopijom masa) i elementarnom analizom. Anti-nociceptivno djelovanje ispitivano je metodom vruće ploče i praćenjem odgovora na bolne podražaje, dok je protuupalno djelovanje evaluirano testom s karageninom. 5-(2-(1*H*-benzo[*d*][1,2,3]triazo-1-il)etil)-1*H*-tetrazol-1-il)(4-aminofenil)metanon (**3d**) i 5-(2-(1*H*-benzo[*d*][1,2,3]triazo-1-il)etil)-1*H*-tetrazol-1-il) (2-hidroksifenil)metanon (**3g**) pokazali su značajno anti-nociceptivno djelovanje. 1-(2-(1-Tosil-1*H*-tetrazol-5-il)etil)-1*H*-benzo[*d*][1,2,3]triazol (**3c**) i 4-5-(2-(1*H*-benzo[*d*][1,2,3]triazo-1-il)etil)-1*H*-tetrazol-1-il sulfonil)benzenamin (**3f**) pokazali su superiorno protuupalno djelovanje u odnosu na druge sintetizirane spojeve. Daljnja istraživanja su nužna kako bi se razjasnio mehanizam djelovanja.

Ključne riječi: sinteza, 1-[2-(1*H*-tetrazol-5-il)etil]-1*H*-benzo[*d*][1,2,3]triazol, nocicepcija, upala

KMCH College of Pharmacy, Coimbatore, Tamilnadu, India

AK College of Pharmacy, Krishnankoil, Tamilnadu, India