SYNTHESIS & ANTI-INFLAMMATORY ACTIVITY OF E-3-ARYLIDENE FLAVANONES

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SUMMARY:

Objective: To synthesize E-3-arylidene flavanones by one pot method and screen their anti-inflammatory activity.

Method: A set of four E-3 arylidene flavanones were synthesized by simple base catalysed condensation of appropriate aryl aldehydes and p-methoxy acetophenone. Screening the anti-inflammatory activity by carageenan induced paw edema method.

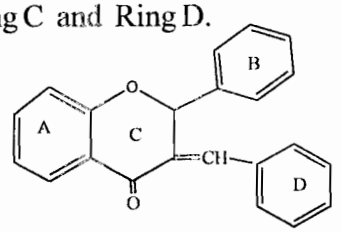
Results: A set of four E-3 arylidene flavanones were synthesized. All four were found to exhibit anti-inflammatory action.

Conclusion: Due to the structural similarity with those of natural flavanones, all the synthesized compounds were expected to exhibit anti-inflammatory activity and all were found to exhibit anti-inflammatory action.

KEY WORDS: E-3 Arylidene flavanone, p-methoxy acetophenone, One- pot method, anti-inflammatory activity, natural flavanone.

INTRODUCTION

3-Arylidene flavanones are also known as flavindogenides. Basic structure of E-3 Arylidene flavanones have four rings, Ring A, Ring B,Ring C and Ring D.



In addition to basic structure of flavanone, E-3 -arylidene flavanone have an extended conjugation at C-3 with carbonyl group. The special feature of long conjugation with the keto groups of flavanone moiety is expected to impart very significant biological activity or this type of cmpounds. On the basis of ^{1}HNMR spectra Keane et al[1] explained the stereochemistry of synthetic E and Z- 3-arylidene flavanones. Chawla et al[2] explained the synthesis of 3-arylidene flavanone uing alkaline medium. Seikel et al[3] described one-pot synthesis of 3-arylidene flavanones. Ray[4] prooved Hesperitin, natural flavanone have anti-oxidant and anti-inflammatory properties.

So here is an attempt made to synthesise a few E-3 -arylidene flavanones by one-pot method and to screen the synthesized compounds for the anti-inflammatory activity

MATERIALS AND METHODS

For the synthesis of proposed compounds, p-methoxyacetophenone have been purchased from Sigma Aldrich chemical company Inc. U.S.A, Benzaldehyde, P-Chloro benzaldehyde,Salicylaldehyde and 3-nitrobenzaldehyde have been purchased from S.D fine chemicals, Mumbai. Carageenan was obtained from Sigma Aldrich chemical compony Inc. U.S.A .

Synthetic Protocol

The proposed cmpounds were synthesized as per the following procedure;[5]

One pot method: To a mixture of p-methoxy acetophenone (1 mM) and aromatic aldehyde (2.5 mM),a warm (45^{0}c) aqueous alcoholic solution of potassium hydroxide(15%) added and stirred the solution to get a uniform solution. The solutionstand for four days in a stoppered condition. Methanol added dropwise to remove turbidity formed on cooling. The separated material washed with cold aqueous alcohol(50 % methanol). Then crystallized from aqueous alcohol.

Biological experimental protocol

To study the anti-inflammatory properties of the synthesized compounds, wistar male

albino rats weighing between150-220g have been selected and carageenan induced paw edema model applied. The rats were divided into six groups having six animals in each group. Four groups received orally, synthesized compounds at a dose of 100 mg/kg in a suspension of 0.5% sodium carboxy methyl cellulose. To one group standard drug Ibuprofen made in 0.5% sodium carboxy methyl cellulose had been administered in the same manner. Remaining group had been given 0.5%sodium carboxy methyl cellulose and treated as control. Edema had been induced after one hour of the compounds administered, by injecting 0.05 ml 1%carageenan suspension subcutaneously into subplantar tissue of right hind foot of rats. Paw volume measured immediately and after 3 hrs of the carageenan injection.

ASSESMENT OF SYNTHESIZED COMPOUNDS

Out of four compounds all four compounds found to had little or more anti-inflammatory activity. Their physical datas are as follows. Ethanol had used as solvent to find out ë -max by U.V spectroscopy. KBr pellets used to measure I.R spectrum and $CDCl_3$ used for ^{1}HNMR spectrum .

Compond A:

χ -max-248 n.m,

I.R(KBr):1674.1c.m $^{-1}$ (C=O),1224.7 and 1176.5 c.m $^{-1}$ (C-O-C), 828.4 c.m $^{-1}$ (C-H def), 1508.2,1421.4 and 1444.6c.m $^{-1}$ (C=C).

1HMR($CDCl_3$ ppm): 6.66-6.7(H-2), 6.8-7 (H-6,H-8), 7.3(CHCl3), 7.8-8.1 (H-3), 7.3-7.4 (H).

Compound B:

χ -max 236 n.m,

I.R(KBr): 1657.7 c.m $^{-1}$(C=O), 1225.7 and 1120.6 c.m $^{-1}$ (C-O-C), 837.0 c.m $^{-1}$ (C-H def), 755.1 c.m $^{-1}$(Cl),1657.7 and 1550.7 - 1463.9 c.m $^{-1}$ (C=C).

1HMR($CDCl_3$ ppm) 6.16-6.2(H-3',H-4'), 6.5-6.6(H-4"), 6.88-6.95(H-.9-8(H-5)8), 7.1-7.2(H-6),7.2-7.3(H-2),7.3 CHCl3, 7.4-7.48 (H-7), 7.6-7.8(H-5"),8-8.1(H-5)

Compound C:

χ–max-242 n.m.

I.R(KBr):1630.7 c.m $^{-1}$(C=O), 1277.8 and1173.6 c.m $^{-1}$(C-O-C),

3032.9 and 3054.1 c.m $^{-1}$(C-H),812.9 and 770.5 c.m $^{-1}$(C-H def), 1630.7 and 1446.5c.m $^{-1}$(C=C), 3426.3c.m $^{-1}$(O-H).

1HMR($CDCl_3$ppm)6.54-6.58(H-2),6.8-7(H-6,H-8), 7.86-7.96(H-5),8.12-8.2(H-B).

Compound D:

χ-max-252 n.m.

I.R(KBr):1669.3 c.m $^{-1}$(C=O), 1173.6 and 1260.4 c.m $^{-1}$(C-O-C),

832.2 and 744.5 c.m $^{-1}$(C-H def), 1669.3 and 1440.7c.m $^{-1}$(C=C), 1419.5c.m $^{-1}$(O-N-O).

1HMR($CDCl_3$ppm)6.56-6.58(H-2),6.9-7(H-6,H-8), 7.8-7.94(H-5),8. 2-8.28(H-B).

RESULTS

As per the synthetic protocol four E-3 Arylidene flavanones have been synthesized and screened their anti-inflammatory activity by carageenan induced paw edema method.The results are reported as mean ± S.D . The obtained data were analysed by unpaired student 't' test. Level of significance was fixed at $p<0.05$. The results of anti-inflammatory activity are shown below:

Statistical analysis

Compound I.D	Edema volume[a] ml(±S.D)	% Edema inhibition[b]
A	0.11(0.015)	37.91%
B	0.16(0.008)	55.15%
C	0.12(0.007)	41.36%
D	0.09(0.004)	31.02%
Std.	0.17(0.009)	58.6%

Edema volume for control (Sodium Carboxy Methyl Cellulose alone)=0.442(0.039)

a=Edema volume expressed as mean (±S.D)of a group.

b= % Edema inhibition calculated by comparing each edema volume with control.

DISCUSSIONS

Four E-3 Arylidene flavanones have been synthesized by one pot method which reduces the tedious multisteps involved in

the synthesis of medicinal compounds.

The results of the assessment of synthesized compounds have good agreement with the datas given in the literature. Due to structural similarity with those of natural flavanones, all the synthesized compounds were expected to exhibit anti-inflammatory activity, as per the studies all four were found to exhibit anti-inflammatory action. The results shows less anti-inflammatory activity than the standard drug namely Ibuprofen. Among the four compounds compound B shows maximum anti-inflammatory activity. Compound D showed least anti-inflammatory activity. Among the four compounds that exhibited anti-inflammatory activity, the compound B shows more activity than others, probably due to the presence of more electronegative atom such as chlorine.

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