IN-VITRO ANTI-INFLAMMATORY ASSAY OF PROP-2-EN-1-ONE DERIVATIVES

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Abstract— In the past 2,3 decades, the literature survey is enriched with progressive findings about the synthesis and pharmacological evaluation of different halosubstituted heterocycles. Prop-2-en-1-one also named as α,β-unsaturated carbonyl system of chalcone and its analogues is recognized as a crucial framework and has been used as a precursor for heterocyclic nuclei with physiological activity. Due to their vital role in synthetic chemistry, it was thought interesting to resynthesize some already developed substituted prop-2-en-1-one derivatives. These synthesized compounds where characterized by elemental analysis, chemical tests and melting points. Some of the titled compounds were evaluated for their anti-inflammatory activities and were found to exhibit moderate to excellent activity.

Index Terms— Anti-inflammatory activity, Chalcones, Substituted prop-2-en-1-one

INTRODUCTION

The property of substances that reduce inflammation is termed anti-inflammatory and substances as anti-inflammatory drugs. Diseases or medical conditions that cause inflammation have a name ending in '-itis' such as Bronchitis (an inflammation of the bronchi), Cystitis (an inflammation of the bladder), Dermatitis (a disease where the skin is inflamed), Uveitis (an inflammation inside the eye), etc. Usually, nonsteroidal anti-inflammatory drugs (NSAIDs) are one of the most common therapeutic groups of agents

used worldwide for the treatment of pain, inflammation, and fever. Most frequently used NSAIDs drugs are salicylates (such as Aspirin), para-aminophenol derivatives (such as Paracetamol), pyrrole derivatives (such as Ketorolac), indole derivatives (such as Ibuprofen), propionic acid derivatives (such as ibuprofen, Ibuprofen and Paracetamol combination, Flurbiprofen, Ketoprofen, Naproxen, Fenamates, and Mefenamic acid), aryl acetic acid derivatives (such as Diclofenac sodium, Diclofenac potassium, Diclofenac and paracetamol combination, Diclofenac and Serratiopeptidase combination), pyrazolones (such as Phenylbutazone and Oxyphenbutazone), others (such as Celecoxib, Rofecoxib, Valdecoxib, and Nimesulide), etc.

However, literature survey shows that Prop-2-en-1-one[1]-[4] also named as α,β-unsaturated carbonyl system of chalcones[5]-[13] belonging to the flavonoid family, are natural and synthetic products that have been reviewed for their wide range of biological activities[14]-[18] as antibacterial, anti-microbial, antifungal, anticancer[19]-[23], anti-tumor, analgesic, antioxidant[24] and anti-inflammatory[25]-[28], antibacterial[29]-[30] agents, etc. Having a varied pharmacological activity and synthetic utility, chalcones are highly attractive molecules because of their simple structure, easy pathway and promising biological[31] activity *in-vivo* as well as *in-vitro*[32] conditions.

MATERIALS AND METHODS:

Previously developed 1,3-phenylprop -2-en-1-one derivatives were re-synthesized and studied for their *in-vitro* anti-inflammatory activity by inhibition of protein denaturation assay.

Synthesis of 1,3-Bis(4-hydroxyphenyl) prop-2-en-1-one (Compound 1):- 4-Hydroxy acetophenone (0.01M) dissolved in ethanol (15ml) was treated with 4-hydroxy benzaldehyde (0.01M) with constant stirring and

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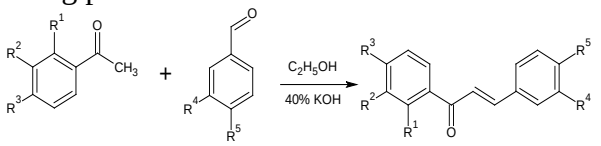
aqueous KOH (40%, 10 ml) was added drop wise. The reaction mixture was stirred at room temperature and kept overnight. The reaction mixture was diluted with water and acidified with 10% HCl. The solid thus separated was filtered and crystallized from acetic acid to get 1,3-Bis(4-hydroxyphenyl)prop-2-en-1-one.

Similarly, compounds 2-10 were also synthesized by using different acetophenones and aldehydes adopting the same procedure followed for compound 1. The newly synthesized compounds where characterized by elemental analysis, chemical tests, TLC and melting points.



R_1 /R_2 /R_3 /R_4 /R_5 = -OH/ -Cl/ -F/ -NMe_2/ -NH_2 /-Br/ -H

Fig1-Scheme of synthesis of prop-2-en-1-one derivatives

Table 1: List of Synthesised prop-2-en-1-one derivatives

Sr. No.	Sample code	Prop-2-en-1-one derivatives	Melting Point (^oC)
1	A	1,3-Bis(4-hydroxyphenyl)prop-2-en-1-one	208-210
2	B	3-(4-Chlorophenyl)-1-(4-hydroxy phenyl)prop-2-en-1-one	130-133
3	C	3-Phenyl-1-(4-hydroxyphenyl)prop-2-en-1-one	160-163
4	D	3-(2-Chlorophenyl)-1-(4-hydroxyphenyl)prop-2-en-1-one	174-176
5	E	3-Phenyl-1-(4-fluorophenyl)prop-2-en-1-one	79-80
6	F	3-(2-Chlorophenyl)-1-(4-fluorophenyl)prop-2-en-1-one	86-90
7	G	3-(3-Bromophenyl)-1-(2-chlorophenyl)prop-2-en-1-one	81-83
8	H	3-[4-(Dimethylamino)phenyl]-1-phenylprop-2-en-1-one	118-120
9	I	1-(3-Aminophenyl)-3-(3-fluorophenyl)prop-2-en-1-one	90-92
10	J	1-(3-Aminophenyl)-3-(3-bromophenyl)prop-2-en-1-one	173-175

Material and Methods

All the reagents used for the analysis of anti-inflammatory studies were of higher analytical grade. The anti-inflammatory activity was carried out *in vitro* by inhibition of protein denaturation assay.

Anti-inflammatory activity:

Protein denaturation test (pain killer)-

Preparation of reference drug (positive control)-

NSAID (ibuprofen) were used as reference drug. Ibuprofen was crushed into fine powder. About 0.2 g of Ibuprofen drug powder was measured using a digital analytical balance and was added to 20.0 ml of distilled water. The solution was mixed well.

Serial dilution from 1000 µg/ml to 0.01µg/ml was performed for 6 sample extract and for reference drugs (prednisolone and ibuprofen). All samples contained 5.0 ml of total volume. Reaction mixtures were prepared using 2.8 ml of phosphate-buffered saline (pH 6.4) and 0.2 ml of egg albumin. Then 2 ml of extract from each different concentration were mixed gently with reaction mixtures. A similar procedure was used for reference drugs (prednisolone and ibuprofen) and they were used.

RESULTS AND DISCUSSION-The results on anti-inflammatory activities of prop-2-en-1-one derivatives (sample A-F) are depicted in Table-2 to 8.

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Table-2: Anti-Inflammatory Activity of Standard Ibuprofen

Sr. no.	Concentration of Ibuprofen (ppm)	Absorbance of blank	Absorbance of sample	Percentage protein denaturation
1	1	0.524	0.305	41.79%
2	2		0.288	45.03%
3	3		0.217	58.58%
4	4		0.173	66.98%
5	5		0.101	80.72%

Table-3: Anti-Inflammatory Activity of Sample A

Sr. no.	Concentration of sample (ppm)	Absorbance of blank	Absorbance of sample	Percentage protein denaturation
1	10	0.524	0.118	77.48%
2	20		0.109	79.19%
3	30		0.091	82.63%
4	40		0.082	84.35%
5	50		0.047	91.03%

Table-4: Anti-Inflammatory Activity of Sample B

Sr. no.	Concentration of sample (ppm)	Absorbance of blank	Absorbance of sample	Percentage protein denaturation
1	10	0.524	0.182	65.26%
2	20		0.163	68.89%
3	30		0.140	73.28%
4	40		0.122	76.71%
5	50		0.089	83.01%

Table-5: Anti-Inflammatory Activity of Sample C

Sr. no.	Concentration of sample (ppm)	Absorbance of blank	Absorbance of sample	Percentage protein denaturation
1	10	0.524	0.186	64.50%
2	20		0.158	69.84%
3	30		0.115	78.05%
4	40		0.089	83.01%
5	50		0.066	87.40%

Table-6: Anti-Inflammatory Activity of Sample D

Sr. no.	Concentration of sample (ppm)	Absorbance of blank	Absorbance of sample	Percentage protein denaturation
1	10	0.524	0.110	79.00%
2	20		0.109	79.19%
3	30		0.095	81.87%
4	40		0.089	83.01%
5	50		0.041	92.17%

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Table-7: Anti-Inflammatory Activity of Sample E

Sr. no.	Concentration of sample (ppm)	Absorbance of blank	Absorbance of sample	Percentage protein denaturation
1	10	0.524	0.296	43.51%
2	20		0.244	53.43%
3	30		0.201	61.64%
4	40		0.189	63.93%
5	50		0.155	70.41%

Table-8: Anti-Inflammatory Activity of Sample F

Sr. no.	Concentration of sample (ppm)	Absorbance of blank	Absorbance of sample	Percentage protein denaturation
1	10	0.524	0.276	47.32%
2	20		0.244	53.43%
3	30		0.204	61.06%
4	40		0.183	65.07%
5	50		0.147	71.94%

Fig 2:Anti-inflammatory activity sample A

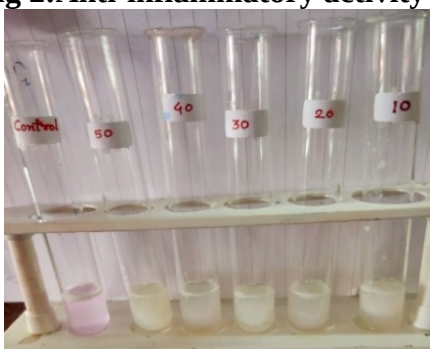


Fig 3:Anti-inflammatory activity sample B

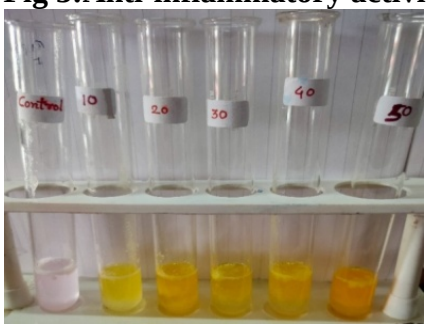


Fig 4:Anti-inflammatory activity sample C

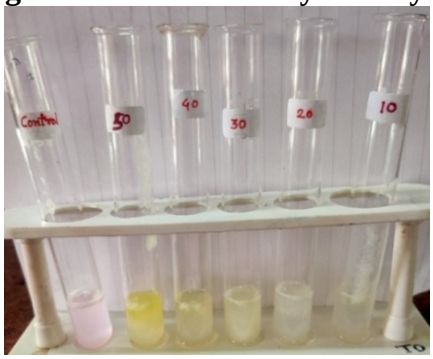


Fig 5:Anti-inflammatory activity sample D

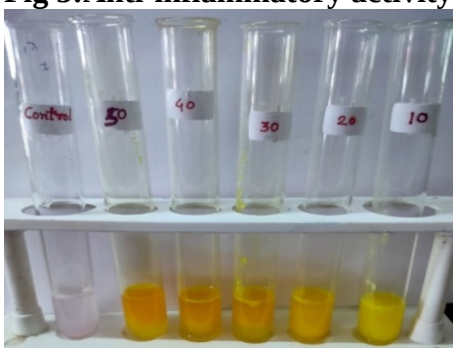


Fig 6:Anti-inflammatory activity sample E

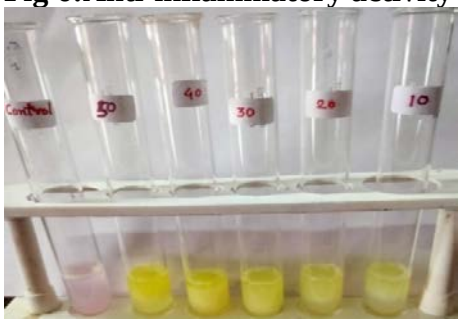
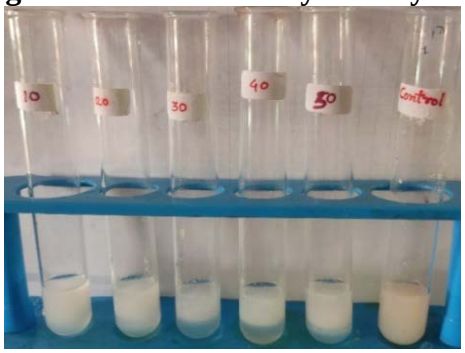


Fig 7:Anti-inflammatory activity sample F



CONCLUSION: The current study reveals the synthesis of substituted prop-2-en-1-one derivatives by a base catalyzed Claisen–Schmidt condensation of substituted acetophenone and substituted aryl aldehydes. Some of the synthesized chalcones were evaluated for their anti-inflammatory activities and were found to exhibit moderate to excellent activity.

Denaturation of proteins is a well-established cause of inflammation. In the present work, the *in-vitro* anti-inflammatory potential of synthesized chalcones was evaluated against denaturation of egg albumin and the results are illustrated in Table 2-8. Most of the compounds were found to have significant anti-inflammatory properties compared to the reference standard Iboprofen, a standard anti-inflammatory drug.

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