

Herbal Interventions for Arthritis: Insights from Aegle Marmelos and Momordica Cymbalaria

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ABSTRACT

Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterized by persistent inflammation, joint degradation, and systemic complications. Current treatment regimens, while effective, often come with adverse effects and limited long-term applicability. Therefore, the exploration of plant-based therapeutic alternatives with minimal toxicity is of significant interest. This study explores the anti-arthritic potential of two medicinal plants, Aegle marmelos and Momordica cymbalaria, widely known for their traditional therapeutic applications. Fruits from both plants were collected, shade-dried, and subjected to successive solvent extraction using petroleum ether, chloroform, ethyl acetate, ethanol, and water. The percentage yield varied with each solvent, with ethanolic extracts showing the highest yield. Phytochemical screening confirmed the presence of bioactive constituents such as alkaloids, flavonoids, phenols, glycosides, saponins, and terpenoids—compounds known for their anti-inflammatory and antioxidant properties. The in vitro anti-arthritic activity was evaluated using protein denaturation assays involving bovine serum albumin and egg albumin. Denaturation of proteins is a primary mechanism in inflammation and rheumatoid arthritis, and agents that prevent this process can serve as potential anti-arthritic drugs. Both plants exhibited dose-dependent inhibition of protein denaturation. Notably, the ethanolic extract of Aegle marmelos demonstrated the highest inhibition (88%) in the bovine serum albumin model, closely comparable to the standard diclofenac sodium (95%). Similarly, Momordica cymbalaria ethanolic extract showed significant inhibition (up to 77%) at 500 µg/mL concentration. These results highlight the therapeutic potential of both plants in managing arthritis through protein stabilization mechanisms. The presence of multiple phytochemicals in the extracts may contribute synergistically to the observed effects. The findings support the ethnomedicinal use of these plants and lay the groundwork for further studies, including in vivo evaluations and isolation of active constituents, to validate and develop effective, plant-based anti-arthritic agents.

Keywords: *Aegle marmelos*, *Momordica cymbalaria*, anti-arthritic activity, protein denaturation, phytochemicals, inflammation, medicinal plants.

1. INTRODUCTION

Rheumatoid arthritis (RA) is a progressive autoimmune disease primarily affecting the synovial joints, leading to chronic inflammation, cartilage degradation, and bone erosion(1). Despite advances in pharmacological therapies, including NSAIDs, corticosteroids, and biologics, the treatment of RA remains challenging due to issues like drug resistance, side effects, and limited accessibility(2). This has driven the exploration of alternative therapies, particularly those derived from natural sources with traditional medicinal value. Medicinal plants have historically been a cornerstone of traditional healthcare systems(3). Their therapeutic potential is largely attributed to the presence of diverse phytochemicals, such as alkaloids, flavonoids, saponins, glycosides, and phenolic compounds, which exhibit anti-inflammatory, antioxidant, and immunomodulatory properties(4). In the context of RA, such bioactive constituents can modulate inflammatory pathways and mitigate oxidative stress, both of which are key contributors to disease progression(5). Among the myriad of medicinal plants, Aegle marmelos (Bael) and Momordica cymbalaria have garnered attention for their broad-spectrum pharmacological properties(6). Aegle marmelos, commonly used in Ayurvedic medicine, has been reported to possess anti-inflammatory,

analgesic, and antioxidant activities. Similarly, *Momordica cymbalaria*, a lesser-known member of the Cucurbitaceae family, has demonstrated promising anti-diabetic and anti-inflammatory effects in preliminary studies(7). However, their specific role in the management of RA, particularly through inhibition of protein denaturation, remains underexplored(8). This study aims to investigate the in vitro anti-arthritis activity of different solvent extracts (petroleum ether, chloroform, ethyl acetate, ethanol, and aqueous) of the fruits of *Aegle marmelos* and *Momordica cymbalaria* (9). The extracts were prepared using Soxhlet extraction and cold maceration techniques, followed by comprehensive phytochemical screening to identify key bioactive constituents(10). In vitro anti-arthritis potential was assessed using protein denaturation assays (bovine serum albumin and egg albumin models), which simulate the denaturation of proteins—a fundamental mechanism in inflammation and autoantigen formation in RA(11). Through a comparative evaluation of the extracts' efficacy and phytochemical composition, this research not only validates the traditional medicinal uses of *Aegle marmelos* and *Momordica cymbalaria* but also provides a scientific basis for their potential integration into complementary RA therapy (12). The findings are expected to contribute toward the development of safer and more affordable anti-arthritis agents derived from natural plant sources(13).

2. EXPERIMENTAL METHODS

2.1 Selection of Medicinal Plants :

Based on an assessment of the relevant literatures, two medicinal plants *Aegle marmelos* and *Momordica Cymbalaria*. were chosen for screening anti arthritis activity in Wistar albino rats(14).

2.2 Preparation of plant material:

After being harvested, the Fruits of *Aegle marmelos* and *Momordica Cymbalaria* were properly cleaned, washed with distilled water, dried in a shaded area, and then powdered using a mechanical mixer. Then it is divided into smaller pieces, sieved with No. 40 and No. 60, then stored in an airtight container and kept at room temperature(15).

2.3 Extraction of the plant material :

With the help of a Soxhlet apparatus, 200 g of finely grounded powders from *Aegle marmelos* and *Momordica Cymbalaria* were extracted for 48 h using a variety of solvents like Petroleum ether, Chloroform, Ethyl acetate and ethanol (from non-polar to polar solvents)(16). The extracts were separated after extraction, condensed by distillation, and dried at room temperature until they formed a viscous solid mass(17). The obtained crude extracts were measured and maintained at 4 °C in sealed glass vials with labels and vacuum desiccators until use(17).

Aqueous Extract

The finely powdered *Aegle marmelos* and *Momordica Cymbalaria* was extracted by cold maceration using water for 15 days(18). The extract was concentrated by surface evaporation followed by vacuum drying. Dry powder was weighed and stored separately in a screw cap vial at 4 °C in a refrigerator for further study (19). Dry powder was weighed and stored separately in a screw cap vial at 4 °C in a refrigerator for further study(20).

2.4 Calculation of Percentage Yield: The percentage yield was calculated by using the formula and is given below(21).

$$\text{Percentage yield} = \frac{\text{weight in grams of extract obtained}}{\text{Weight in grams of plant material taken}} \times 100$$

3. PHYTOCHEMICAL SCREENING OF AEGLE MARMELOS AND MOMORDICA CYMBALARIA:

Any plant that includes compounds with therapeutic properties or compounds that can be utilized as building blocks for semi-synthetic pharmaceuticals is considered a medicinal plant(21). These phytochemicals, which are non-nutrients found in plants, act as defence mechanisms for the plants against microbial diseases or pest infestations(22). Thus, the phytochemical components of the various extracts of *Aegle marmelos* and *Momordica Cymbalaria* were screened(23).

Methodology for phytochemical analysis :

Tests for alkaloids

Several drops of diluted hydrochloric acid were added to a small quantity of the solvent-free extract before being agitated and filtered(24). Various alkaloid reagents, including: were used to thoroughly test the filtrate (25).

a. Mayer's reagent

The filtrate was treated with Mayer's reagent (potassium mercury solution). The appearance of a cream color indicated the presence of alkaloids(26).

b. Dragendorff's reagent

A little amount of the filtrate was treated with Dragendorff's reagent (potassium bismuth iodide solution)(27). The appearance of reddish-brown precipitate indicated the presence of alkaloids(28).

c. Hager's reagent

The test sample was treated with Hager's reagent (picric acid). The appearance of yellow precipitate indicated the presence of alkaloids(29).

d. Wagner's reagent

A little amount of the extract was treated with Wagner's reagent (iodine and potassium iodide solution)(30). The appearance of reddish-brown precipitate indicated the presence of alkaloids (31).

Test for carbohydrates

Dissolve a small quantity of the extract in 4 mL of distilled water and filter(32). The filtrate was subjected to Molisch's test for the presence of carbohydrates(33).

a. Molisch's Test

To 2 mL of extract, 1 mL of α -naphthol solution was added, and concentrated sulphuric acid was added through the sides of the test tube(34). The formation of the violet colour ring at the junction of two liquids indicated the presence of carbohydrates(35).

Tests for glycosides

Another small portion of the extract was hydrolyzed with diluted hydrochloric acid for a few min in a heated water bath and the hydrolysate was subjected to Legal's and Borntrager's tests to detect the presence of different glycosides(36).

a. Legal's test

The hydrolysate was treated with 1 mL of pyridine, a few drops of sodium nitroprusside solution, and sodium hydroxide solution to make it alkaline(37). The presence of cardenolide glycosides is shown by the colour change from pink to red(38).

b. Borntrager's test

To the hydrolysate, 1 mL of chloroform was added and shaken well(39). The chloroform layer was separated and to this equal amount of dilute ammonia solution was added. The appearance of pink color in the ammonical layer indicated the presence of anthraquinone glycosides(40).

c. Keller kiliani test

When a pinch of the extract was dissolved in glacial acetic acid, a few drops of ferric chloride solution were added, followed by the addition of concentrated sulphuric acid, formation of a red ring at the junction of two liquids indicated the presence of glycosides(41).

Test for phytosterol

a. Libermann- Burchard's Test

A small amount of the extract was dissolved in a few drops of glacial acetic acid(42). 3 mL of acetic anhydride was added, followed by adding a few drops of concentrated sulfuric acid. The appearance of bluish-green color shows the presence of phytosterol(43).

b. Salkowski Test

A small quantity of the extract was dissolved in chloroform and the resulting solution was then shaken with a few drops of concentrated sulfuric acid. The appearance of bluishgreencolor shows the presence of phytosterol(44).

Tests for fixed oils and fats

a. Saponification test

A small amount of extract was mixed with a few drops of 0.5 N alcoholic potassium hydroxide solution and a drop of phenolphthalein(45). The mixture was cooked for 1-2 h in a water bath. Fixed oils and fats were present when soap formed or when alkali was partially neutralised(46).

b. Spot test

A small quantity of the extract was pressed between two filter papers. Oil stains on the paper indicated the presence of fixed oil(47).

Test for saponins

a. Foam test

1 g of the extract was shaken vigorously with 20 mL distilled water in a graduated cylinder for 15 min. a 1 cm layer of foam indicated the presence of saponins(48).

Tests for tannins and phenolic compounds

A small quantity of the extract was dissolved in water, warmed, and filtered. The resulting filtrate was used for the following tests (49).

a. Ferric chloride test

Neutral ferric chloride solution was used to treat a tiny portion of the filtrate. The presence of phenols was revealed by the emergence of violet colour(50).

b. Gelatine test

A small amount of the filtrate was treated with a 1 % w/v solution of gelatine in water containing 10 % sodium chloride. The appearance of the cream precipitate indicated the presence of phenolic compounds(51).

c. Lead acetate test

A small amount of the filtrate was treated with a 10 % lead acetate solution. The appearance of white precipitate indicated the presence of phenolic compounds(52).

Tests for proteins and amino acids

A small quantity of the extract was shaken with a few mL of water and the resulting mixture was subjected to the following tests:

a. Millon's test

When the test sample was treated with Millon's reagent (Mercuric nitrate solution), the formation of white precipitate indicated the presence of proteins(53).

b. Ninhydrin test

When the test sample was treated with a 0.1 % w/v solution of ninhydrin in n-butanol, the appearance of the violet or purple color indicated the presence of an amino acid(54).

c. Biuret test

When the test sample was treated with an equal volume of 5 % sodium hydroxide solution and 1 % copper sulphate reagent, the appearance of the pink to purple color indicated the presence of proteins and free amino acids(55).

Test for flavonoids

A small quantity of the extract was shaken with a few mL of water and the resulting mixture was subjected to the following tests

a. Shinoda's test

A small quantity of the test sample was dissolved in 5 mL of alcohol (95%) and treated with a few drops of concentrated hydrochloric acid and 0.5 g of magnesium turnings(56).

The development of pink color within a minute indicated the presence offlavonoids(57).

b. Fluorescence test

A few mg of the extract was dissolved in alcohol and a drop of the resulting solution was placed on Whatman filter paper and observed under UV light. The appearance of fluorescence indicated the presence of flavonoids(58).

Test for lignin

A small quantity of the extract was treated with a few drops of phloroglucinol and hydrochloric acid. The appearance of pink or red color indicated the presence of lignin(59).

Tests for detection of triterpenes

a. Salkowski's test

A small quantity of the extract was taken in a dry test tube, added a few tin granules and 1 mL of thionyl chloride, and shaken well. The appearance of a pink color indicated the presence of triterpenes(60).

b. Libermann-Burchard's Test

To the solution of extract, 1 mL of acetic anhydride and acetic acid were added, followed by a few drops of concentrated sulfuric acid. A ray of colours from violet changing through purple to brown or blue indicated the presence of triterpenes(61).

4. IN VITRO ANTI ARTHRITIS ACTIVITY

PROTEIN DENATURATION METHOD:

PRINCIPLE:

Protein denaturation is the process in which the protein lose their secondary and tertiary structure by application of external stress, heat, compounds (acid, base) and mineral salts (62). Proteins lose their biological function. This protein denaturation is well documented in cause of inflammation. The ability of extract to inhibit protein denaturation will be studied by this method(63).

Inhibition of protein denaturation (bovine serum albumin):

Denaturation of tissue protein is one of the well-documented causes of inflammatory and arthritic diseases. Production of the auto antigen in certain arthritic diseases may be due to denaturation of protein in vitro(64).

METHODS:

The following three solutions were used.

Test solution:

0.5 ml of test solution consists of 0.45 ml of BSA (5% w/v) and 0.05 ml of extracts in various concentrations (100, 200, 300, 400, and 500 µg/ml) (65).

Test control solution:

0.5 ml of test control solution consists of 0.45 ml of BSA (5% w/v) and 0.05 ml of distilled water (66).

Standard solution:

0.5 ml of standard solution consists of 0.45 ml of BSA (5% w/v) and 0.05 ml of diclofenac sodium solution (100, 200, 300, 400, and 500 µg/ml)(67,68).

The pH of the above solutions was adjusted to 6.3 using a small amount of 1N HCl. The samples were incubated at 37°C for 20 min and heated at 57°C for 3 min which were cooled, and 2.5 ml of phosphate buffer (pH 6.3) was added to it. Control represents 100% proteins(69,70). After cooling, their absorbance was measured at 660 nm using pure blank. Diclofenac sodium (standard drug) was used as reference drug and treated as such for determination of absorbance(71,72).

The percentage inhibition of protein denaturation was calculated as follows:

(Abs control - Abs sample)

$$\text{Percentage inhibition} = \frac{\text{Abs control} - \text{Abs sample}}{\text{Abs control}} \times 100$$

METHODOLOGY:

The following three solutions were used.

Test solution:

5 ml of test solution consists of 0.2 ml of egg albumin and 2.8 ml of phosphate buffer saline and 2 ml of in various concentrations of extracts (100, 200, 300, 400, and 500 µg/ml)(73,74).

Test control solution:

5 ml of test control solution consists of 0.2 ml of egg albumin and 2.8 ml of phosphate buffered saline and 2 ml of distilled water(75,76).

Standard solution:

5 ml of standard solution consists of 0.2 ml of egg albumin and 2.8 ml of phosphate buffer saline and diclofenac (100,200, 300, 400, and 500 µg/ml)(77,78).

The pH of the above solutions was adjusted to 6.4 using a small amount of 1N HCl(79,80). The samples were incubated at 37°C for 20 min and heated at 70°C for 5 min denaturations, and the results were compared with standard diclofenac sodium(81,82).

After cooling, their absorbance was measured at 660 nm using pure blank(83,84,85). Diclofenac sodium (standard drug) was used as reference drug and treated as such for the determination of absorbance(86,87,88). The percentage inhibition of protein denaturation was calculated as follows: (89)

(Abscontrol - Abs sample)

$$\text{Percentage inhibition} = \frac{\text{Abs control} - \text{Abs sample}}{\text{Abs control}} \times 100$$

Proteinase inhibition assay: Anti-trypsinase activity

In this assay, 2ml sample solution was comprised of 60µl trypsin (0.6µg), 1ml test extract (100, 200, 300, 400, and 500 µg/ml) and 1ml tris HCl buffer (25mM pH 7.4) (90,91,92). The blank solution contained tris HCl buffer while the standard solution contained Diclofenac Sodium instead of the extract solution(93,94). All solutions were incubated at 37°C for 5 min. afterwards 1ml casein (0.8% w/v) added(95). Again, solutions were incubated for 20 min(96,97). Perchloric acid (2ml, 70%v/v) was added to stop the reaction followed by centrifugation at 5000 rpm for 5 min(98). The absorbance of the supernatant was determined at 280 nm(99). The test was carried out and the percentage inhibition of proteinase enzyme was calculated(100). The percentage of Proteinase inhibition assay was calculated as follows:

(Abscontrol -Abs sample)

$$\text{Percentage inhibition} = \frac{\text{Abs control} - \text{Abs sample}}{\text{Abs control}} \times 100$$

(Abs control)

RESULTS AND DISCUSSION:

During the phytochemical analysis, the different polarity of phytoconstituents was separated from the fruit powder of *Aegle marmelos* and *Momordica Cymbalaria* by using solvents such as petroleum ether, chloroform, ethyl acetate, and ethanol, and then performing successive extractions with a Soxhlet apparatus. This was done in order to determine which phytoconstituents were present in the fruit powder. The particulars regarding the polarity and solubility of the metabolites found in the plant were revealed by successive extractive values.

This table contains an explanation of the percentage yield of the extracts.

Table :1 Properties of different extracts from the fruits of *Aegle marmelos* and *Momordica Cymbalaria*

S. No.	Extracts	Colour		Consistency		Percentage Yield (w/w)	
		AM	MC	AM	MC	AM	MC
1	Petroleum ether	Greenish black	Brownish	Semi-solid	Semi-solid	5	4
2	Chloroform	Pale green	Pale brown	Semi-solid	Semi-solid	4	4.5
3	Ethyl acetate	Dark green	Dark brown	Semi solid	Semi solid	8	9
4	Ethanol	Dark green	Dark brown	Semi solid	Semi solid	11	13
5	Aqueous	Dark green	brown	Semi solid	Semi solid	4	5

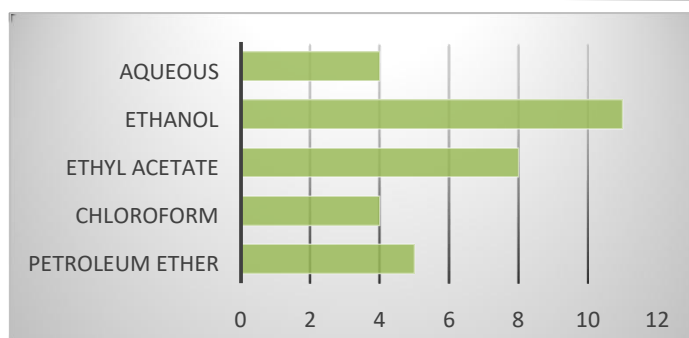


Fig: 3Percentage yield of different extracts of *Aegle marmelos*

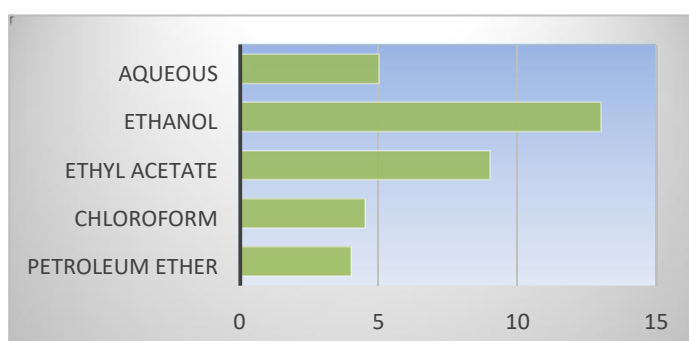


Fig: 4Percentage yield of different extracts of *Momordica Cymbalaria*

The phytochemical components of the different extracts of *Aegle marmelos* and *Momordica Cymbalaria* were screened. The findings of the phytochemical screening are displayed in the given Table. In *Aegle marmelos* petroleum ether extract revealed the presence of lipids, proteins, phytosterols, fixed oils, and carbohydrates. Alkaloids, carbohydrates, glycosides, phytosterol, fixed oils, and tannins were all present in the chloroform extract. Carbohydrates, proteins, phytosterol, tannins, flavonoids, and triterpenes were all detected in ethyl acetate extract. Proteins, alkaloids, carbohydrates, phytosterols, saponins, tannins, flavonoids, and triterpenes were all present in the ethanolic extract. Carbohydrates, proteins, saponins, flavonoids, lignin, and triterpenes were all detected in the aqueous extract.

While the primary and secondary metabolites from this preliminary research were discovered in *Momordica Cymbalaria* phytochemical screening. Proteins, amino acids, steroids, glycosides, saponin, fixed oils, and lipids were present in the petroleum ether extract. Alkaloids, steroids, fixed oils, and fats were the only secondary metabolites that the chloroform extracts revealed to be present. Alkaloids, carbohydrates, proteins, amino acids, steroids, phenols, tannins, flavonoids, glycosides, saponins, and terpenoids were all detected in the ethanol and ethyl acetate extracts. More secondary metabolites than primary metabolites were detected in the aqueous extracts. Carbohydrates, steroids, phenols, tannins, flavonoids, saponins, lignins, and terpenoids were among the phytoconstituents.

Table:2 Results of preliminary Phytochemical screening of *Aegle marmelos* and *Momordica Cymbalaria*

S. No.	Constituents	Observation									
		PEE		CE		EAE		EE		AE	
		AM	MC	AM	MC	AM	MC	AM	MC	AM	MC
1	Alkaloids	-	-	+	+	-	+	+	+	-	-

2	Carbohydrates	+	-	+	-	+	+	+	+	+	+
3	Proteins & amino acids	-	+	+	-	+	+	+	+	+	-
4	Steroids	+	+	+	+	+	+	+	+	-	+
5	Phenols	-	-	+	-	+	+	+	+	-	+
6	Tannins	-	-	+	-	+	+	+	+	-	+
7	Flavonoids	-	-	-	-	+	+	+	+	+	+
8	Glycosides	-	+	+	-	-	+	-	+	-	-
9	Saponins	-	+	-	-	-	+	+	+	+	+
10	Fixed oil and fats	+	+	+	+	-	-	-	-	-	-
11	lignin	-	-	-	-	-	-	-	-	+	+
12	Terpenoids	-	-	-	-	+	+	+	+	+	+

Table: 3 Anti-arthritis activity of *Aegle marmelos* by bovine serum albumin method

Treatment	Concentration	Test Absorbance	Control	% inhibition
	(µg/ml)		Absorbance	
PEEAM	100	0.061	0.084	27
	200	0.053	0.081	34
	300	0.049	0.079	37
	400	0.047	0.029	62
	500	0.040	0.022	81
CEAM	100	0.064	0.081	20

	200	0.056	0.079	29
	300	0.052	0.039	33
	400	0.045	0.031	45
	500	0.043	0.029	48
EAEAM	100	0.062	0.084	26
	200	0.055	0.079	30
	300	0.051	0.038	34
	400	0.046	0.031	48
	500	0.038	0.022	72
EEAM	100	0.051	0.081	37
	200	0.049	0.031	56
	300	0.047	0.030	58
	400	0.045	0.027	66
	500	0.017	0.009	88
AEAM	100	0.062	0.084	26
	200	0.061	0.084	27
	300	0.051	0.081	37
	400	0.046	0.031	41
	500	0.041	0.029	48
Diclofenac sodium	100	0.052	0.039	33
	200	0.051	0.038	34
	300	0.046	0.031	48

	400	0.044	0.027	62
	500	0.043	0.022	95

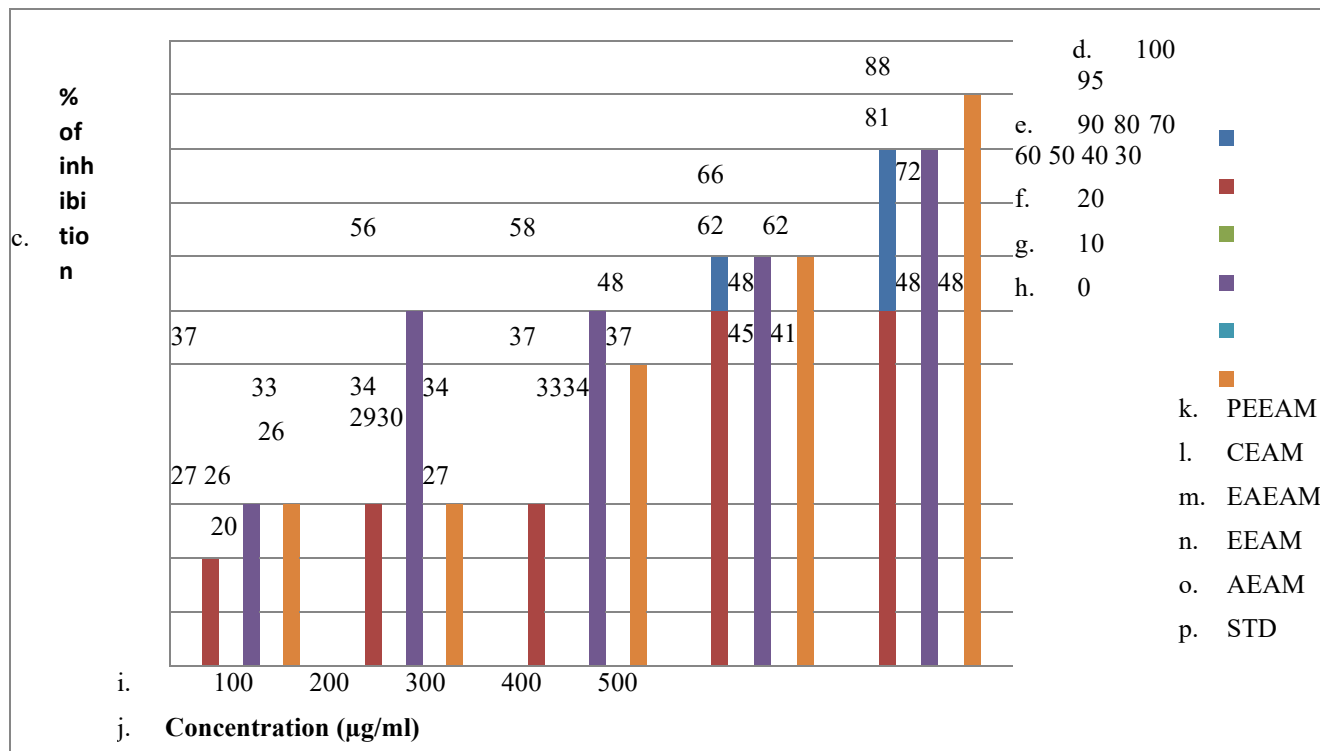


Fig:1. 1 Anti-arthritic activity of *Aegle marmelos* by bovine serum albumin

Table: 4 Anti-arthritic activity of *Momordica Cymbalaria* by bovine serum albumin method

Treatment	Concentration (µg/ml)	Test Absorbance	Control Absorbance	% inhibition
PEEAM	100	0.077	0.084	8
	200	0.067	0.081	17
	300	0.064	0.079	18
	400	0.044	0.029	51
	500	0.035	0.022	59
CEAM	100	0.066	0.081	18
	200	0.054	0.079	31

	300	0.053	0.039	35
	400	0.047	0.031	51
	500	0.046	0.029	58
EAEAM	100	0.067	0.084	20
	200	0.058	0.079	26
	300	0.051	0.038	34
	400	0.046	0.031	48
	500	0.035	0.022	59
EEAM	100	0.057	0.081	29
	200	0.048	0.031	54
	300	0.047	0.030	56
	400	0.043	0.027	59
	500	0.015	0.009	66
AEAM	100	0.066	0.084	21
	200	0.062	0.084	26
	300	0.052	0.081	35
	400	0.043	0.031	38
	500	0.041	0.029	41
Diclofenac sodium	100	0.052	0.039	33
	200	0.051	0.038	34
	300	0.046	0.031	48
	400	0.044	0.027	62
	500	0.043	0.022	95

	400	0.047	0.029	62
	500	0.041	0.022	86
CEAM	100	0.066	0.081	18
	200	0.055	0.079	30
	300	0.052	0.039	33
	400	0.046	0.031	48
	500	0.044	0.029	51
EAEAM	100	0.066	0.084	21
	200	0.057	0.079	27
	300	0.051	0.038	34
	400	0.045	0.031	45
	500	0.039	0.022	77
EEAM	100	0.053	0.081	34
	200	0.048	0.031	54
	300	0.047	0.030	56
	400	0.044	0.027	62
	500	0.017	0.009	88
AEAM	100	0.064	0.084	23
	200	0.061	0.084	27
	300	0.054	0.081	33
	400	0.046	0.031	48
	500	0.044	0.029	51

Diclofenac sodium	100	0.052	0.039	33
	200	0.051	0.038	34
	300	0.046	0.031	48
	400	0.044	0.027	62
	500	0.043	0.022	95

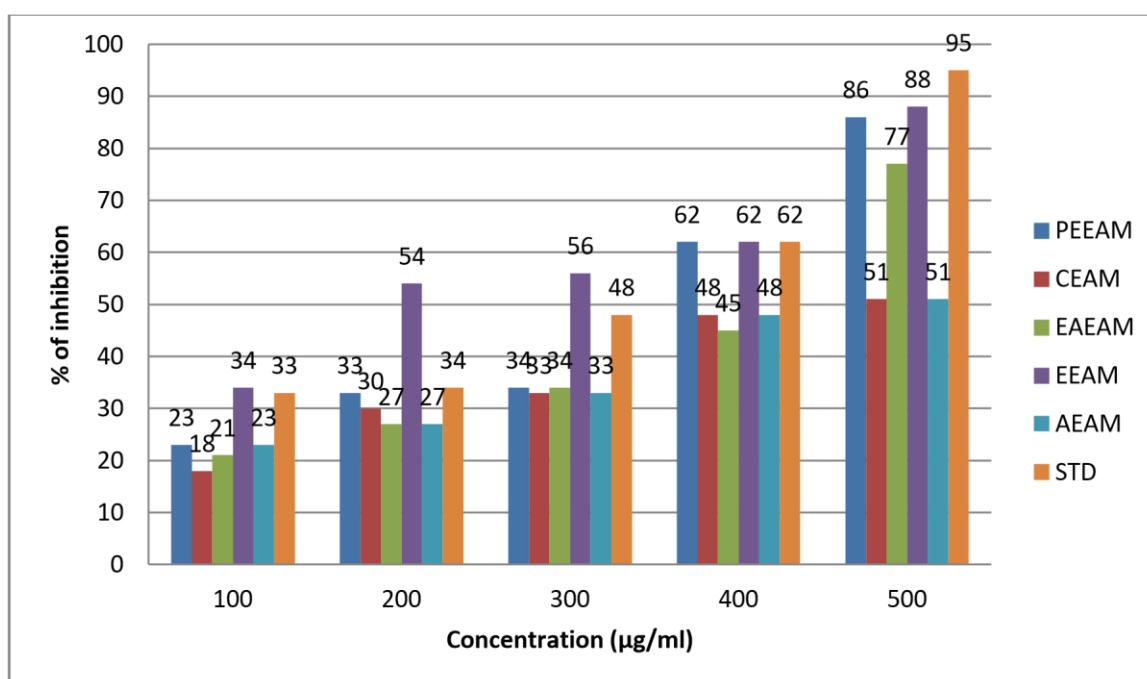


Fig: 3 Anti-arthritis activity of *Aegle marmelos* by egg albumin method

Table: 6 Anti-arthritis activity of *Momordica Cymbalaria* by egg albumin method

Treatment	Concentration (µg/ml)	Test Absorbance	Control Absorbance	% inhibition
PEEAM	100	0.074	0.084	11
	200	0.064	0.081	20
	300	0.062	0.079	21
	400	0.049	0.029	68
	500	0.038	0.022	72

CEAM	100	0.064	0.081	20
	200	0.054	0.079	31
	300	0.052	0.039	33
	400	0.048	0.031	54
	500	0.047	0.029	62
EAEAM	100	0.067	0.084	20
	200	0.057	0.079	27
	300	0.050	0.038	31
	400	0.046	0.031	48
	500	0.037	0.022	68
EEAM	100	0.056	0.081	30
	200	0.049	0.031	56
	300	0.047	0.030	58
	400	0.045	0.027	66
	500	0.016	0.009	77
AEAM	100	0.064	0.084	23
	200	0.062	0.084	26
	300	0.055	0.081	32
	400	0.044	0.031	41
	500	0.042	0.029	44
Diclofenac sodium	100	0.052	0.039	33
	200	0.051	0.038	34

	300	0.046	0.031	48
	400	0.044	0.027	62
	500	0.043	0.022	95

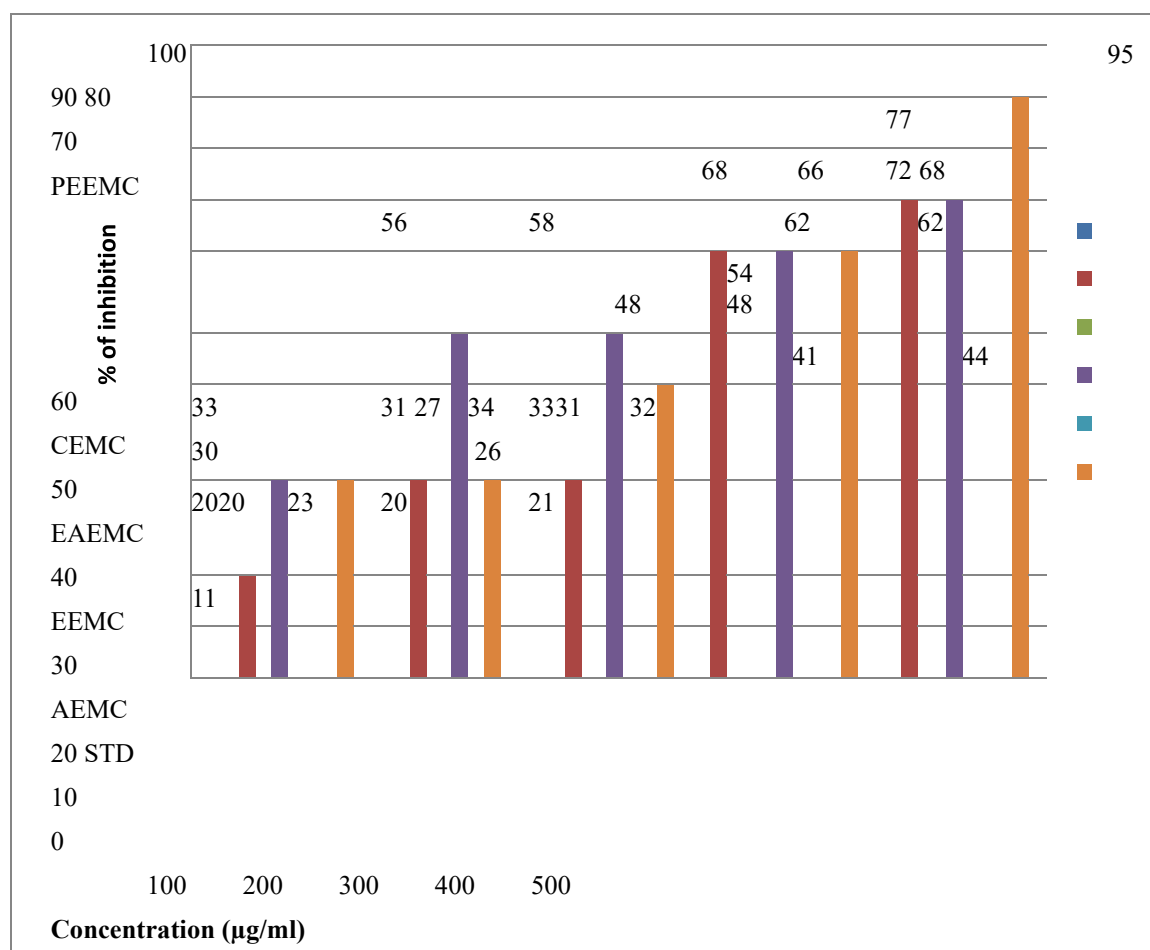


Fig. 4 Anti-arthritic activity of *Momordica cymbalaria* by egg albumin method

5. CONCLUSION

This study evaluated the anti-arthritic potential of *Aegle marmelos* and *Momordica cymbalaria* through in vitro experiments, particularly focusing on their efficacy in preventing protein denaturation and enzyme activity—key contributors to the pathogenesis of rheumatoid arthritis (RA). RA is a chronic autoimmune disorder characterized by persistent inflammation, joint degradation, and systemic complications. While current treatments are effective, they often have side effects and limited long-term benefits, prompting the need for safer, plant-based alternatives. The fruits of both plants were subjected to successive solvent extraction using petroleum ether, chloroform, ethyl acetate, ethanol, and water. Ethanol extracts yielded the highest recovery, indicating efficient extraction of polar bioactive constituents. Phytochemical screening revealed the presence of multiple therapeutically significant compounds—alkaloids, flavonoids, tannins, saponins, phenols, glycosides, steroids, and triterpenes—which are known for their anti-inflammatory, antioxidant, and immunomodulatory activities. In vitro anti-arthritic assays were conducted using bovine serum albumin (BSA) and egg albumin denaturation models, both of which mimic the protein unfolding processes linked to inflammation and autoantigen formation in RA. Both *Aegle marmelos* and *Momordica cymbalaria* extracts demonstrated significant, dose-dependent inhibition of protein denaturation. Notably, the ethanolic extract of *Aegle marmelos* showed the highest inhibition rate of 88% at 500 µg/mL, which is close to the 95% inhibition observed with diclofenac sodium, the standard drug. Similarly, *Momordica cymbalaria*'s ethanolic extract achieved 77% inhibition at the same concentration. Additionally, the proteinase inhibition assay indicated the ability of both plants to

inhibit enzymatic activity that contributes to tissue degradation in arthritic conditions. Again, ethanolic extracts exhibited superior activity, aligning with the presence of potent polyphenolic and triterpenoid compounds. Among the tested solvents, ethanol proved most effective in extracting a wide range of bioactive constituents, and thus, ethanolic extracts consistently outperformed others in anti-arthritic evaluations. Non-polar solvents like petroleum ether and chloroform were less effective both in phytochemical richness and biological activity. The observed effects are likely due to the synergistic action of phytochemicals. Flavonoids and phenolics inhibit inflammatory mediators and oxidative stress, while saponins and tannins stabilize cell membranes and prevent protein unfolding. Such multi-target effects make plant-based therapies valuable alternatives or complements to conventional drugs. In conclusion, both *Aegle marmelos* and *Momordica cymbalaria* possess substantial anti-arthritic properties, particularly in their ethanol-extracted forms. The *in vitro* models validate their ability to inhibit protein denaturation and enzymatic activity, essential steps in the inflammatory cascade of RA. These results support their traditional medicinal use and encourage further *in vivo* studies and compound isolation for potential pharmaceutical development. Integrating traditional plant knowledge with modern pharmacology may lead to safer, more accessible treatments for chronic inflammatory conditions like rheumatoid arthritis.

REFERENCES

- [1] A current view on inflammation. *Nat Immunol.* 2017;18(825). <https://doi.org/10.1038/ni.3798>.
- [2] Aletaha, D., Neogi, T., Silman, A. J., et al. (2010). Rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis & Rheumatism*, 62(9), 2569-2581.
- [3] Anosike, C.A., Obidoa, O., Ezeanyika, L.U.S., 2012. Membrane stabilization as a mechanism of the anti-inflammatory activity of methanol extract of garden egg (*Solanum aethiopicum*). *DARU Journal of Pharmaceutical Sciences* 20, 1–7.
- [4] Aparna, V., Dileep, K.V., Mandal, P.K., Karthe, P., Sadasivan, C., Haridas, M., 2012. Antiinflammatory property of n-hexadecanoic acid: structural evidence and kinetic assessment. *Chemical Biology & Drug Design* 80, 434–439
- [5] Awuchi CG. Medicinal plants: The medical, food, and nutritional biochemistry and uses. *IJAAR.* 2019;5:220–41.
- [6] Bailey, K.L. The bioherbicide approach to weed control using plant pathogens. In *Integrated Pest Management*; Academic Press: Cambridge, MA, USA, 2014; pp. 245– 266.
- [7] Bennett JM, Reeves G, Billman GE, Joachim P, Sturmberg. Inflammation Nature’s way to efficiently respond to all types of challenges: Implications for Understanding and managing “the epidemic” of chronic diseases. *Front Med.* 2018;5:1–30.
- [8] Bishop, F. L., Lewith, G. T., & Ernst, E. (2012). *Herbal medicine for the treatment of osteoarthritis: A systematic review.* *Rheumatology*, 51(4), 55-64.
- [9] Brima EI. Toxic elements in different medicinal plants and the impact on human health. *Int J Environ Res Public Health.* 2017;14:1209.
- [10] Burgers, L. E., Welsing, P. M., & van der Heijde, D. M. (2014). Imaging in rheumatoid arthritis: Insights from the EULAR imaging workshop. *Rheumatology*, 53(6), 1024-1033.
- [11] Cedillo-Cortezano M, Martinez-Cuevas LR, López JA, Barrera López IL, EscutiaPerez S, Petricevich VL. Use of medicinal plants in the process of wound healing: a literature review. *Pharmaceuticals.* 2024 Feb 27;17(3):303.
- [12] Chaudhary, M., & Patel, N. (2018). Phytochemical screening and antioxidant activity of *Momordica cymbalaria*. *Pharmacognosy Journal*, 10(6), 1234-1240.
- [13] Cheng, F.; Cheng, Z. Research progress on the use of plant allelopathy in agriculture and the physiological and ecological mechanisms of allelopathy. *Front. Plant Sci.* 2015, 6, 1020. [CrossRef] [PubMed] .
- [14] Chowdhary, N., Kaur, M., Singh, A., Kumar, B., 2014. Wound healing activity of aqueous extracts of *Ficus religiosa* and *Ficus benghalensis* leaves in rats. *Indian Journal of Research in Pharmacy and Biotechnology* 2, 1071–1081.
- [15] Cordeau, S.; Triolet, M.; Wayman, S.; Steinberg, C.; Guillemain, J.P. Bioherbicides: Dead in the water? A review of the existing products for integrated weed management. *Crop Prot.* 2016, 87, 44–49. [CrossRef]
- [16] David A, Chinedu E. The importance of toxicity testing. *JPBS.* 2013;4:146–8.
- [17] Dayan, F.E.; Cantrell, C.L.; Duke, S.O. Natural products in crop protection. *Bioorg. Med. Chem.* 2009, 17, 4022–4034. [CrossRef] .

- [18] De Menezes Patricio Santos, C.C., Salvadori, M.S., Mota, V.G., Costa, L.M., De Almeida, A.A.C., De Oliveira, G.A.L., Costa, J.P., De Sousa, D.P., De Freitas, R.M., De Almeida, R.N., 2013. Antinociceptive and antioxidant activities of phytol in vivo and in vitro models. *Neuroscience Journal*. 2013, 949452.
- [19] Devi DR, Lakshna SS, Parvathi SV, Hari BV. Investigation of wound healing effect of topical gel of Albizia amara leaves extract. *South African Journal of Botany*. 2018 Nov 1;119:400-9.
- [20] El-Darier, S.M.; Abdelaziz, H.A.; El-Dien, M.H.Z. Effect of soil type on the allelotoxic activity of Medicago sativa L. residues in Vicia faba L. agroecosystems. *J. Taibah Univ. Sci*. 2014, 8, 84–89. [CrossRef]
- [21] Emery MA, Eitan S. Drug-specific differences in the ability of opioids to manage burn pain. *Burns*. 2020;46:503–13.
- [22] Eslaminezhad S, Moradi F, Hojjati MR. Evaluation of the wound healing efficacy of new antibacterial polymeric nanofiber based on polyethylene oxide coated with copper nanoparticles and defensin peptide: An in-vitro to in-vivo assessment. *Heliyon*. 2024 Apr 30;10(8).
- [23] Feldmann, M., & Maini, R. N. (2001). Role of cytokines in rheumatoid arthritis. *Arthritis Research & Therapy*, 3(2), 11-18.
- [24] Ferreira, I.C.F.R., Baptista, P., Vilas-Boas, M., Barros, L., 2007. Free-radical scavenging capacity and reducing power of wild edible mushrooms from Northeast Portugal: Individual cap and stipe activity. *Food Chemistry* 100, 1511–1516.
- [25] Goldring, M. B. (2012). *Osteoarthritis and Cartilage: The Role of Inflammation*. *Current Opinion in Rheumatology*, 24(1), 8-13. <https://doi.org/10.1097/BOR.0b013e32834c57b0>
- [26] González-Gay, M. A., Gonzalez-Juanatey, C., & García-Porrúa, C. (2017). Cardiovascular risk in rheumatoid arthritis: The role of inflammation. *Rheumatology International*, 37(3), 345-353.
- [27] Gupta, R., Kumar, M., & Sharma, A. (2015). Phytochemical and pharmacological aspects of Aegle marmelos (Bael). *Journal of Ethnopharmacology*, 174, 70-85. <https://doi.org/10.1016/j.jep.2015.07.021>
- [28] Heap, I.; Duke, S.O. Overview of glyphosate-resistant weeds worldwide. *Pest. Manag. Sci*. 2018, 74, 1040–1049. [CrossRef] .
- [29] Hochberg, M. C., Altman, R. D., April, K. T., et al. (2012). *2012 American College of Rheumatology recommendations for the management of rheumatoid arthritis*. *Arthritis Care & Research*, 64(5), 625-639. <https://doi.org/10.1002/acr.21641>
- [30] Hossen, K.; Das, K.R.; Asato, Y.; Teruya, T.; Kato-Noguchi, H. Allelopathic activity and characterization of allelopathic substances from Elaeocarpus floribundus Blume leaves for the development of bioherbicides. *Agronomy* 2022, 12, 57. [CrossRef] .
- [31] Hunter, D. J., & Bierma-Zeinstra, S. (2019). *Osteoarthritis*. *Lancet*, 393(10182), 1745-1759. [https://doi.org/10.1016/S0140-6736\(19\)30417-9](https://doi.org/10.1016/S0140-6736(19)30417-9)
- [32] Islam, M.S.; Zaman, F.; Iwasaki, A.; Suenaga, K.; Kato-Noguchi, H. Isolation and identification of three potential phytotoxic compounds from Chrysopogon aciculatus (Retz.) Trin. *Acta Physiol. Plant* 2021, 43, 56. [CrossRef] .
- [33] James, O., Victoria, I.A., 2010. Excision and incision wound healing potential of Saba florida leaf extracts in Rattus norvegicus. *International Journal of Pharmaceutical and Biomedical Research* 1, 101–107.
- [34] Kalimuthu, K., Prabakaran, R., 2013. Preliminary phytochemical screening and GCMS analysis of methanol extract of Ceropegia pusilla. *International Journal of Research in Applied Natural and Social Sciences* 1, 49–58
- [35] Kaur J, Kumar V, Sharma K, Kaur S, Gat Y, Goyal A, et al. Opioid peptides: an overview of functional significance. *Int J Pept Res Ther*. 2020;26:33–41
- [36] Khan MSA, Ahmad I. Herbal medicine: current trends and future prospects: New Look to Phytomedicine Elsevier; 2019. p. p3–13.
- [37] Kirtikar, K. R., & Basu, B. D. (2001). *Indian Medicinal Plants*, Vol. I–IV. Dehradun: Oriental Enterprises.
- [38] Kirtikar, K.R., & Basu, B.D. (2005). *Indian Medicinal Plants*, Vol. 2. Dehradun: International Book Distributors.
- [39] Kishore N, Kumar P, Shanker K, Verma A. Overcome, Human disorders associated with inflammation and the evolving role of natural products to overcome. *Eur J Med Chem*. 2019;179:272–309.
- [40] Klareskog, L., Catrina, A. I., & Paget, S. (2009). Rheumatoid arthritis. *The Lancet*, 373(9664), 659-672.
- [41] Kohila, K., Deepika, S., Priyadarshini, Sujatha, 2013. Phytopharmacological properties of Albizia: Review. *International Journal of Pharmacy and Pharmaceutical Sciences* 5, 70–73

- [42] Kumar, P., & Singh, R. (2015). Chemical constituents and medicinal uses of *Momordica* species. *International Journal of Pharmacognosy and Phytochemical Research*, 7(2), 290-295.
- [43] Kumar, S., et al. (2021). A comprehensive review on *Aegle marmelos* (L.) Corrêa: Its traditional uses, phytochemistry, and pharmacological profile. *Journal of Ethnopharmacology*, 273, 113957. <https://doi.org/10.1016/j.jep.2021.113957>
- [44] Kumar, S., Sharma, N., & Pathak, S. (2017). Anti-inflammatory and analgesic effects of *Momordica cymbalaria*. *International Journal of Pharmacognosy*, 6(3), 54-59.
- [45] Lal UR, Lal S. Bioactive molecules from Indian medicinal plants as possible candidates for the management of neurodegenerative disorders: Natural products-from bioactive molecules to human health. IntechOpen; 2020. <https://doi.org/10.5772/intechopen.92043>.
- [46] Mahdi, H. J., Khan, N. A. K., Asmawi, M. Z. B., Mahmud, R., & A/L Murugaiyah, V. (2018). In vivo anti-arthritic and anti-nociceptive effects of ethanol extract of *Moringa oleifera* leaves on complete Freund's adjuvant (CFA)-induced arthritis in rats. *Integrative medicine research*, 7(1), 85-94. <https://doi.org/10.1016/j.imr.2017.11.002>
- [47] Mani S, Duraipandian C, Chidambaram SB. Analgesic, anti-inflammatory and acute oral toxicity profile of leaf and bark extracts of *Albizia procera*. *BMC Complementary Medicine and Therapies*. 2022 Feb 25;22(1):50.
- [48] Mar, W., Tan, G.T., Cordell, G.A., Pezzuto, J.M., Jurcic, K., Redl, K., Steinke, B., Wagner, H., 1991. Biological activity of novel macrocyclic alkaloids (Budmunchiamines) from *Albizia amara* detected on the basis of interaction with DNA. *Journal of Natural Products* 54, 1531-1542.
- [49] Martins P, Fonseca JE. How to investigate: Pre-clinical rheumatoid arthritis. *Best Practice & Research Clinical Rheumatology*. 2019;101438
- [50] McInnes, I. B., & Schett, G. (2011). *The Pathogenesis of Rheumatoid Arthritis*. *New England Journal of Medicine*, 365(23), 2205-2219. <https://doi.org/10.1056/NEJMra1004965>
- [51] McInnes, I. B., & Schett, G. (2011). The pathogenesis of rheumatoid arthritis. *The New England Journal of Medicine*, 365(23), 2205-2219.
- [52] Mendes, I.D.S.; Rezende, M.O.O. Assessment of the allelopathic effect of leaf and seed extracts of *Canavalia ensiformis* as post emergent bioherbicides: A green alternative for sustainable agriculture. *J. Environ. Sci. Health Part B* 2014, 49, 374- 380. [CrossRef] .
- [53] Mensah ML, Komlaga G, Forkuo AD, Firempong C, Anning AK, Dickson RA. Toxicity and safety implications of herbal medicines used in Africa. *Herb Med*. 2019;63:849-1992.
- [54] Midwood, K.S., Williams, L.V., Schwarzbauer, J.E., 2004. Tissue repair and the dynamics of the extracellular matrix. *The International Journal of Biochemistry & Cell Biology* 36, 1031-1037.
- [55] Mujawdiya PK, Kapur S. Screening of antioxidant and α -glucosidase inhibitory activities of Indian medicinal plants. *Curr EnzymInhib*. 2020;16(2):145-54.
- [56] Mushtaq, W.; Ain, Q.; Siddiqui, M.B.; Hakeem, K.R. Cytotoxic allelochemicals induce ultrastructural modifications in *Cassia tora* L. and mitotic changes in *Allium cepa* L.: A weed versus weed allelopathy approach. *Protoplasma* 2019, 256, 857-871. [CrossRef] [PubMed] .
- [57] Neogi, T. (2011). *Clinical practice: Osteoarthritis*. *The New England Journal of Medicine*, 364(12), 1271-1280. <https://doi.org/10.1056/NEJMcp1012191>
- [58] Nirbhavane, P., Sharma, G., Singh, B., Khuller, G. K., Goni, V. G., Patil, A. B., & Katare, O. P. (2018). Preclinical Explorative Assessment of Celecoxib-Based Biocompatible Lipidic Nanocarriers for the Management of CFA-Induced Rheumatoid Arthritis in Wistar Rats. *AAPS PharmSciTech*, 19(7), 3187-3198. <https://doi.org/10.1208/s12249-018-1148-3>
- [59] Oguntibeju OO. Medicinal plants with anti-inflammatory activities from selected countries and regions of Africa. *J Inflamm Res*. 2018;11:307-17.
- [60] Orwa, C., Mutua, A., Kindt, R., Jamnadass, R., Anthony, S., 2009. Agroforestry Database: A Tree Reference and Selection Guide Version. Available from. <http://www.worldagroforestry.org/sites/treedbs/treedatabases.asp>, Accessed date: January 2017.
- [61] Oyedapo, O.O., Akinpelu, B.A., Akinwunmi, K.F., Adeyinka, M.O., Sipeolu, F.O., 2010. Red blood cell membrane stabilizing potentials of extracts of *Lantana camara* and its fractions. *International Journal of Plant Physiology and Biochemistry* 2, 46-51.
- [62] Patel, J., Patel, B., Banwait, H., Parmar, K., Patel, M., 2010. Formulation and evaluation of topical aceclofenac gel using different gelling agent. *International Journal of Drug Development and Research* 3, 156-164

- [63] Patil KR, Mahajan UB, Unger BS, Goyal SN, Belemkar S, Surana SJ, et al. Animal models of inflammation for screening of anti-inflammatory drugs: implications for the discovery and development of phytopharmaceuticals. *Int J Mol Sci.* 2019;20:4367.
- [64] Plenge, R. M., Cotsapas, C., Davies, L. et al. (2005). Two independent alleles at 6q23 and 5p15 are associated with rheumatoid arthritis. *Nature Genetics*, 37(5), 515-517.
- [65] Poole, A. R. (2012). *Osteoarthritis as a Disease of Cartilage and Bone. The Journal of Clinical Investigation*, 122(6), 2052-2062. <https://doi.org/10.1172/JCI60219>
- [66] Posinasetty, B., Chikatipalli, R., Chenchula, S., Kuttiappan, A., G, S., G N A, L., & Audinarayana, N. (2023). Anti-arthritis efficacy of Bombax ceiba ethanolic extract in a murine model for rheumatoid arthritis using in vivo, in vitro and radiological analysis. *Bioinformation*, 19(8), 833–839. <https://doi.org/10.6026/97320630019833>
- [67] Prajapati, N. D., Purohit, S. S., Sharma, A. K., & Kumar, T. (2003). *A Handbook of Medicinal Plants*. Agrobios, India.
- [68] Pramod C, Sudhakaran N, Harindran J. Antiinflammatory effects of Lablab purpureus Linn in polyphenolic fraction from methanolic leaf extract on experimental animal model. *Pharma Innov J.* 2020;9(2):338-44.
- [69] Praveen, P., Thippeswamy, S., Mohana, D.C., Manjunath, K., 2011. Antimicrobial efficacy and phytochemical analysis of Albizia amara (Roxb.) Boiv. An indigenous medicinal plant against some human and plant pathogenic bacteria and fungi. *Journal of Pharmacy Research* 4, 832–835.
- [70] Ramchandani, U., Sangameswaran, B., 2013. Formulation and evaluation of topical gel of Ketoprofen using different polymers. *International Journal of Pharmaceutical & Biological Archive* 4, 323–326.
- [71] Raychaudhuri, S., Sandor, C., & Stahl, E. A. et al. (2012). Five amino acids in three HLA molecules explain most of the association between MHC and seropositive rheumatoid arthritis. *Nature Genetics*, 44(3), 291-296.
- [72] Redfern, J., Kinninmonth, M., Burdass, D., Verran, J., 2014. Using soxhlet ethanol extraction to produce and test plant material (essential oils) for their antimicrobial properties. *Journal of Microbiology & Biology Education* 15, 45–46.
- [73] Rob, M.; Hossen, K.; Iwasaki, A.; Suenaga, K.; Kato-Noguchi, H. Phytotoxic activity and identification of phytotoxic substances from Schumannianthus dichotomus. *Plants* 2020, 9, 102. [CrossRef] [PubMed] 46. Hossen, K.; Das, K.R.; Okada, S.; Iwasaki, A.; Suenaga, K.; Kato-Noguchi, H. A
- [74] Romanik, G., Gilgenast, E., Przyjazny, A., Kamiński, M., 2007. Techniques of preparing plant material for chromatographic separation and analysis. *Journal of Biochemical and Biophysical Methods* 70, 253–261.
- [75] Sabu, M. C., & Kuttan, R. (2004). Antidiabetic activity of *Aegle marmelos* and its relationship with its antioxidant properties. *Indian Journal of Physiology and Pharmacology*, 48(1), 81–88.
- [76] Sangeetha M, Chamundeeswari D, Babu CS, Rose C, Gopal V. Attenuation of oxidative stress in arthritic rats by ethanolic extract of Albizia procera benth bark through modulation of the expression of inflammatory cytokines. *J Ethnopharmacol.* 2020;250:112435.
- [77] Sawhney G, Kaur S, Bhagat A, Ahmed Z. Medicinal plants and their role in inflammation: A close look on future drug discovery. In: *Botanical leads for drug discovery*: Springer; 2020. p. 137–58.
- [78] Saxena, A.K., & Saxena, R. (2013). Phytochemical and pharmacological properties of *Momordica cymbalaria* — A review. *Journal of Pharmacognosy and Phytochemistry*, 2(4), 10-15.
- [79] Sharma, P. V. (1996). *Dravyaguna Vijnana*, Vol. II. Chaukhamba Bharati Academy, Varanasi. Shubha, G., Govindaraju, B., Satyanarayan, N.D., Manjunatha, K.S., 2014. Antibacterial activity of different solvent extracts of Albizia amara. *Indian Journal of Scientific Research* 5, 9–12
- [80] Shukr, M.H., Metwally, G.F., 2013. Evaluation of topical gel bases formulated with various essential oils for antibacterial activity against methicillin-resistant *Staphylococcus aureus*. *Tropical Journal of Pharmaceutical Research* 12, 877–884.
- [81] Siddiqui, W. A., Khan, A. W., & Rizvi, M. (2014). *Aegle marmelos*: A plant with a multitude of medicinal properties. *Pharmacognosy Research*, 6(1), 1-10. <https://doi.org/10.4103/0974-8490.123084>
- [82] Singh, S., Gupta, M. M., & Mishra, R. K. (2017). *Aegle marmelos* (Bael) as an effective therapeutic agent: A review. *International Journal of PharmTech Research*, 10(2), 47-52.
- [83] Soderlin, M., Ronnelid, J., & Jacobsson, L. (2007). Infections as triggers for the development of rheumatoid arthritis. *Scandinavian Journal of Rheumatology*, 36(1), 1-6.
- [84] Soltys, D.; Krasuska, U.; Bogatek, R.; Gniazdow, A. Allelochemicals as bioherbicides present and perspectives.

In Herbicides Current Research and Case Studies in Use; Price, A.J., Kelton, J.A., Eds.; In Tech: Rijeka, Croatia, 2013; pp. 517–542.

- [85] Sousa, De A.T.O., De Melo Buriti Vasconcelos, J., Oliveira Soares, M.J.G., 2012. Software image tool 3.0 as an instrument for measuring wounds. *Journal of Nursing UFPE online* 6, 2569–2573
- [86] Srivastava V, Kumar VS, Panwar S, Deep P, Verma S. A brief review on phytopharmacological reports on *Albizia procera*. *Asian J Pharm Sci.* 2020;6:144–9.
- [87] Suruse, P.B., Bodele, S.B., Duragkar, N.J., Saundankar, Y.G., 2013. In vitro evaluation of antioxidant activity of *Albizia lebbeck* bark. *International Journal of Biological Science and Ayurveda Research* 1, 6–17.
- [88] Syversen, S. W., Kristensen, J. H., & Gaarder, P. I. (2004). Smoking and citrullinated proteins in the pathogenesis of rheumatoid arthritis. *Rheumatology International*, 24(6), 348-354.
- [89] Thawabteh, A.; Juma, S.; Bader, M.; Karaman, D.; Scrano, L.; Bufo, S.A.; Karaman, R. The biological activity of natural alkaloids against herbivores, cancerous cells and pathogens. *Toxins* 2019, 11, 656. [CrossRef] [PubMed] .
- [90] Tiwari, A., Kumar, S., & Sharma, R. (2014). Anti-Arthritic Activity of *Momordica cymbalaria* in Animal Models. *Journal of Traditional and Complementary Medicine*.
- [91] Upadhyay, R.K., Balekar, N., Jain, D.K., Jain, N.K., 2013. Evaluation of wound healing activity of stem bark of *Albizia lebbeck*. *International Journal of Pharmaceutical & Biological Archive* 4, 672–677.
- [92] Ustuner, T.; Sakran, L.; Almhemed, K. Effect of herbicides on living organisms in the ecosystem and available alternative control methods. *Int. J. Sci. Res. Publ.* 2020, 10, 622–632. .
- [93] van der Linden, M. P., Huizinga, T. W., & Klareskog, L. (2010). Risk factors for the development of rheumatoid arthritis. *Current Opinion in Rheumatology*, 22(3), 256-261.
- [94] Verma, A., Verma, R., & Kumar, S. (2018). Pharmacological and therapeutic properties of *Momordica cymbalaria*: A review. *Journal of Medicinal Plants Research*, 12(17), 222-228.
- [95] Versteeg, H.H., Heemskerk, J.W.M., Levi, M., Reitsma, P.H., 2013. New fundamentals in hemostasis. *The American Psychological society*. 93 pp. 327–358.
- [96] Wakefield, R. J., Durigova, M., & Paleolog, E. (2015). Ultrasound in rheumatoid arthritis. *Rheumatology*, 54(1), 12-16.
- [97] Yadava, R.N., Tripathi, P., 2000. Chemical examination and anti-inflammatory action of the extract from the stem of *Albizia procera*. *Research Journal of Chemistry and Environment* 4, 57–60.
- [98] Zhang, C., Zhang, W., Shi, R., Tang, B., & Xie, S. (2019). *Coixlachryma-jobi* extract ameliorates inflammation and oxidative stress in a complete Freund's adjuvant-induced rheumatoid arthritis model. *Pharmaceutical biology*, 57(1), 792–798. <https://doi.org/10.1080/13880209.2019.1687526>
- [99] Zvaifler, N. J., & Firestein, G. S. (2000). The Pathogenesis of Rheumatoid Arthritis: A Review. *Journal of Clinical Rheumatology*, 6(1), 10-22. <https://doi.org/10.1097/00124743-200002000-00003>