



(REVIEW ARTICLE)



Chemical constituents and pharmacological activities of *Mirabilis jalapa*- A review

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International Journal of Biological and Pharmaceutical Sciences Archive, 2021, 01(02), 034–045

Publication history: Received on 13 January 2021; revised on 01 February 2021; accepted on 03 February 2021

Article DOI: <https://doi.org/10.30574/ijbpsa.2021.1.2.0303>

Abstract

Mirabilis jalapa was used traditionally in the treatment of kidney infections, as diuretic, tonic, cathartic, purgative and emetic. The phytochemical screening of the extracts of the leaves and stems of the *Mirabilis jalapa* revealed the presence of tannins, alkaloids, flavonoids, phenolic compounds, carbohydrates, terpenes, glycosides, saponins, protein, cardiac glycosides, steroids and emodin. The previous pharmacological studies revealed that *Mirabilis jalapa* possessed wide range of pharmacological and therapeutic effects included antimicrobial, antiparasitic, dermatological, anticancer, anti-inflammatory, analgesic, antidiabetic, antihistaminic, immune-modulatory, antispasmodic and many other pharmacological effects. The chemical constituents, nutritional, pharmacological and therapeutic effects of *Mirabilis jalapa* were discussed in the current review.

Keywords: *Mirabilis jalapa*; constituents; traditional uses; pharmacology; therapeutic; toxicology

1. Introduction

Medicinal plant research received much attention as it brings to light the numerous unknown medicinal virtues especially of plant origin which needs evaluation on modern scientific lines such as chemical analysis, pharmacological investigation, pharmacokinetic and pharmacodynamic studies and clinical trials. *Mirabilis jalapa* was used traditionally in the treatment of kidney infections, as diuretic, tonic, cathartic, purgative and emetic. The phytochemical screening of the extracts of the leaves and stems of the *Mirabilis jalapa* revealed the presence of tannins, alkaloids, flavonoids, phenolic compounds, carbohydrates, terpenes, glycosides, saponins, protein, cardiac glycosides, steroids and emodin. The previous pharmacological studies revealed that *Mirabilis jalapa* possessed wide range of pharmacological and therapeutic effects included antimicrobial, antiparasitic, dermatological, anticancer, anti-inflammatory, analgesic, antidiabetic, antihistaminic, immune-modulatory, antispasmodic and many other pharmacological effects. The current review will highlight the chemical constituents, nutritional, pharmacological and therapeutic effects of *Mirabilis jalapa*.

1.1. Synonyms

Jalapa congesta, *Jalapa officinalis*, *Mirabilis ambigua*, *Mirabilis jalapa* var. *jalapa*, *Mirabilis jalapa* subsp. *lindheimeri*, *Mirabilis lindheimeri*, *Mirabilis jalapa* var. *lindheimeri*, *Mirabilis pedunculata*, *Mirabilis planiflora*, *Mirabilis pubescens*, *Mirabilis suaveolens*, *Mirabilis xalapa* and *Nyctagojalapae* [1].

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1.2. Taxonomic classification

Kingdom: Plantae, Subkingdom: Viridiplantae, Infrakingdom: Streptophyta, Superdivision: Embryophyta, Division: Tracheophyta, Subdivision: Spermatophytina, Class: Magnoliopsida, Superorder: Caryophyllanae, Order: Caryophyllales, Family: Nyctaginaceae, Genus: *Mirabilis*, Species: *Mirabilis jalapa* [2].

1.3. Common names

Arabic: Shab Al-Leil, Al-Shab A-Ildhareef, Lala Abbas; Chinese: zimo li; English: beauty-of-the-night, false jalap, four-o'clock; French: belle-de-nuit, Italian: bella di notte; Japanese: oshiroi-bana; Persian: Lalehabbasi; Spanish: buenastardes; Swedish: underblomma; Turkish: Akşamsefas [3].

1.4. Distribution

There is some disagreement about where it came from originally (tropical America, probably of Peru, Mexico, Chile, or India). Today it was widely distributed throughout the tropics of the world [4-5].

1.5. Description

Herbs annual, to 1 m tall. Roots tuberous, black or black-brown. Stems is erect, branched, glabrous, cylindrical, or slightly pubescent, inflated on nodes. Petiole 1-4 cm, leaf, 3-15 × 2-9 cm, blade ovate or ovate-triangular, base truncate or cordate, margin entire, apex acuminate. Flowers are several clustered at apex of branches, fragrant; pedicel 1-2 mm. Perianth red, purple, white, yellow, or variegated, tube 2-6 cm, limb 2.5-3 cm in diameter, opening in late afternoon, closing next morning. Stamens 5, filaments slender, exserted; anther globose. Fruits are globose, black, diameter 5-8 mm, coriaceous, ribbed and plicate. Endosperm white mealy [6-7].

1.6. Traditional uses

Leaves were employed for poulticing abscesses and boils. Juices of the leaves were used in treatment of skin allergy, and in earaches in children. Leaves infusion was applied topically to reduce swelling in conditions like bone fractures or twisting. Decoction of *Mirabilis Jalapa* was used orally as diuretic and in the treatment of kidney infections. Stems were used as tonic. The root of *Mirabilis Jalapa* was used traditionally as cathartic, purgative, emetic, in the treatment of abnormal accumulation of pus and or liquid and for inflamed and enlarged lymph-nodes [8-11].

The seed powder was used in Zaire externally for infected wounds. In Latin America the roots were used as a purgative and emetic. In Malagasy the plant was used to treat intestinal pains. In South Africa the roots were used as a purgative and the flowers were reputed to emit an odour at night which stupefies or drives away mosquitoes [12].

1.7. Part used

Leaves, stems and roots were used medicinally [8-12].

1.8. Physicochemical characteristics

Studying of physicochemical parameters of the ethanolic extracts of leaf of *Mirabilis jalapa* showed that the percent (w/w) of the total ash was 15.15, acid insoluble ash 4.57, water soluble ash 3.75, water soluble extractive value 26.22, alcohol soluble extractive value 21.81 and ether soluble extractive value 24.94% [13]. The physicochemical parameter of powder of the whole *Mirabilis jalapa* were: loss on drying 12.41% ± 0.005, total ash 11.81% ± 0.001, water soluble ash 5.06% ± 0.001, acid insoluble ash 0.41% ± 0.001, alcohol soluble 11.02% ± 0.007, water soluble materials 18.63% ± 0.007 and ether soluble materials 7.17% ± 0.007 [14].

The seeds produced 3.0% oil, of 0.70 g/ml density, 26.10 dynes/cm surface tension, and 169.5 millipoise viscosity at 20.5° C. The determined iodine value was 80 and saponification value 172 [15].

1.9. Chemical constituents

The preliminary phytochemical screening of the extracts of the leaves and stems revealed the presence of tannins, alkaloids, flavonoids, phenolic compounds, carbohydrates, terpenes, glycosides, saponins, protein, cardiac glycosides, steroids and emodin [13, 16-21].

(Z)-3-hexenyl acetate, β-myrcene, (Z)-ocimene, benzyl benzoate, monoterpene (E)-β-ocimene were the major fragrance component in the plant volatiles. Investigation of the emission of (E)-β-ocimene, showed an evening-specific maximum (1700-2000 pm), while, the emission of (Z)-3-hexenyl acetate reached its maximum 3 h later [22].

The *Mirabilis jalapa* leaves extract contained hydrocarbons 17.8%, ketones 18.0%, alcohols 12.1%, sterols 21.2% and acids 7.0%, oxymethylantraquinone, trigonelline, arabinose, galactose and beta-sitosterol [23-24].

The amount of essential elements in *Mirabilis jalapa* leaves (mg/kg) were: Mn 0.42, Fe 5.02, Zn 1.19, Pb 0.04, Cr 0.14 and Cu 0.067 and in the stems were: Pb 0.13, Zn 1.74, Cu 0.58, Cr 0.13, Mn 0.72 and Fe 4.88 [16].

The seeds showed high protein content (11.0 ± 0.75 g/100 seed). Amino acid analyses of the total protein isolates showed that it consisted of 17 amino acids of which 9 were essential [25].

The analysis of fatty acids constituents of the seed oil showed that they included palmitic acid 18.3%, oleic acid 55.3%, linoleic acid 11.5% and linolenic acid 14.9% [26].

Many betaxanthins pigments (indicaxanthin, vulgaxanthin-I, miraxanthin-I, -II, -III, -IV, -V and -VI) were identified in the flowers of *Mirabilis jalapa* [27].

The compounds isolated from the dichloromethane extract of *Mirabilis jalapa* tubers powder were (%): 2-butoxyethyl acetate 0.47; 2,3,5,6-tetramethylpyrazine 0.20; 3,6-dioxo-2,7-disilaooctane 1.83; 2-butenedioic acid 0.88; urea 1.52; 3,7-dioxo-2,8-disilanonane 2.98; 4-hydroxyquinoline 4.68; pyrimidine 1.09; isosteviol 5.22; n-pentadecanoic acid 0.83; hexadecanoic acid 10.98; octadecan-1-ol 0.83; linoleic acid 10.47; oleic acid 24.74; cyclopentasiloxane 0.90; cholestan-16-one 1.08; lukianol 1.29; pregn-5-en-20-one 1.15; dihydrostigmasterol 3.15 and benzene 1.23%. However, the compounds isolated from the methanol extract of *Mirabilis jalapa* tubers powder were (%): 9,12-octadecadienoic acid 0.83; 9,17-octadecadienal 0.18; 2-methyl-Z,Z-3,13-octadecadienol 0.84; 1,5,9,13-tetradecatetraene 0.61; cholest-5-en-24-one 10.58; stigmasterol 18.29, β -sitosterol 60.73 and cholestane 4.32% [28].

3,3'-Methylenebis(4-hydroxycoumarin); N-D-alpha-phenylglycine; laminaribitol and 3-(4-(dimethylamino)cinnamoyl)-4-hydroxycoumarin were isolated from the *Mirabilis jalapa* whole plant methanol extract [29].

Rotenoids (mirabijalone A, B, C and D, 9-O-methyl-4-hydroxyboeravinone B, boeravinone C and F, 1,2,3,4-tetrahydro-1-methylisoquinoline-7,8-diol), 9-O-methyl-4-hydroxyboeravinone B, boeravinone C and F, and 1,2,3,4-tetrahydro-1-methylisoquinoline-7,8-diol were identified in the roots of *Mirabilis jalapa* [30].

The compounds isolated from the roots of the plant were identified as astragaloside II, astragaloside II, astragaloside IV, astragaloside VI, flazin, 4'-hydroxy-2, 3-dihydroflavone 7-beta-D-glucopyranoside, ginglycolipid A, 3, 4-dihydroxybenzaldehyd, p-hydroxybenzaldehyde, beta-sitosterol and daucosterol [31]. The roots of *Mirabilis jalapa* also contained glycerin monoecisate, boeravinone C, mirabijalone A, chrysophanol, stigmasterol, and chrysophanol [32].

A fatty acid, 8-hydroxyoctadeca-*cis*-11,14-dienoic acid was isolated from the seed oil of *Mirabilis jalapa* [33].

Quantitative analysis showed that *Mirabilis Jalapa* leaves contained 0.034mg/kg alkaloids [16]. The flavonoid content was 4.41 ± 0.02 mg /gram of the methanolic extract of *Mirabilisjalapa* aerial parts [34]. The total phenolic contents of the extracts of *Mirabilis jalapa* tubers was varied from 21.45 to 364.6mg gallic acid equivalent (GAE)/g dried extract and the total flavonoid from 5.2 to 71.6 mg quercetin/g dried extract, respectively [28]. The total phenolic content and total flavonoid content of the ethyl acetate extract of the seed epicarp were 4.24 mg GAE/g and 0.39 mg RE/g of dry powder weight respectively [35].

The phenolic compounds identified in the extract of *Mirabilis jalapa* tubers powder were: ferulic acid, procyanidin derivative, ferulic acid derivative, p-coumaryl-ester, Q-3-O-rhamnoside, dicaffeic acid, rutin and pgl-3-O-glucoside [28]. Polyphenolic amide: *N-trans-feruloyl 4'-O-methyldopamine* was also isolated the methanolic extract of *Mirabilis jalapa* [36].

2. Pharmacological effects

2.1. Antimicrobial effects

The antimicrobial effect of ethanolic extract of *Mirabilis Jalapa* leaves was studied against Gram positive and Gram negative bacteria and against two fungi. The zones of growth inhibition of the ethanolic leaves extract were:

Staphylococcus aureus 11.1mm, *Salmonella typhi* 13.5mm, *Escherichia coli* 15.0mm, *Pseudomonas aeruginosa* 15.5mm, *Penicilliumnotatum* 35.0mm and *Rhizopusstolonifer* 30mm [16].

N-trans-feruloyl 4'-O-methyldopamine, polyphenolic compound isolated the methanolic extract of *Mirabilis jalapa* showed moderate activity against multidrug-resistant (MDR) *Staphylococcus aureus* [36].

Two antimicrobial peptides, designated as Mj-AMP1 and Mj-AMP2, were isolated from *Mirabilis jalapa* seeds, they exhibited a broad spectrum antifungal activity, they were active against 13 plant pathogenic fungi. Concentrations required for 50% inhibition of fungal growth vary from 6 to 300 micrograms/ml for the first peptide, and from 0.5 to 20 micrograms/ml for the second peptide. Both peptides were also active against two Gram-positive bacteria but showed no effect against Gram-negative bacteria [37].

The aqueous and methanolic seeds powder extracts and their combination (1:2 mixture of the aqueous and methanol extracts) at dilutions of 40, 4, 0.4 and 0.04 mg/ml, were tested for antibacterial effect against *Staphylococcus aureus*, *Streptococcus pyogenes*, *Escherichia coli*, *Enterobacter* sp., *Vibrio cholerae*, *Shigella flexneri* and *Salmonella typhi*. The aqueous extract possessed good growth inhibition against all the bacteria except *Enterobacter* sp., while the methanol extract showed good inhibition against all except *Staphylococcus aureus*. The combination of extracts showed good inhibition of all the bacteria to a dilution of 4 mg/ml, and inhibition of *Staphylococcus aureus* at 0.4 mg/ml [12].

The antibacterial activity of the aqueous, ethanol, methanol, chloroform and petroleum ether, leaves extracts were tested for their antibacterial activity against *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Bacillus cereus*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Lactobacillus acidophilus*, *Salmonella typhi* and *Shigella dysenteriae*. Aqueous, chloroform and petroleum ether extracts displayed the minimal inhibition while all the ethanolic and methanolic extracts showed good antibacterial activity against the selected pathogens (zone of growth inhibition 11-15mm against all the tested bacteria, except against *Streptococcus pneumoniae* 8mm) [38].

The antimicrobial effects of acetone, chloroform, ethanol and methanol extracts of the leaves of *Mirabilis jalapa* were investigated against *Bacillus subtilis*, *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Aspergillus flavus*, *Aspergillus fumigatus*, *Aspergillus niger* and *Aspergillus terreus*. The methanol extract at 500µg/disc extract exerted the largest zone of growth inhibition (21mm) against *Staphylococcus aureus* and the highest inhibition of fungal radial mycelial growth (97.5% at 500µg/ml medium) against *Aspergillus flavus*. The methanol extract showed the lowest MIC against *Staphylococcus aureus* (39µg/ml) and *Aspergillus flavus* (45µg/ml) [19].

The investigation of the antibacterial effects of aqueous and alcoholic *Mirabilis jalapa* leaves extracts showed that 0.5 mg/ml concentration was effective inhibitor of growth of *Staphylococcus aureus*, *Escherichia coli* and *Proteus mirabilis* [18].

The antibacterial potential of the methanolic extract of *Mirabilis jalapa* aerial parts was examined against Gram positive and Gram negative organisms. The extract displayed significant activity against all the tested microorganisms with MIC of 1mg/ml [34, 39].

The methanol, acetone, diethyl ether and chloroform extracts of different *Mirabilis jalapa* varieties were tested for antibacterial activities against Gram negative bacteria (*Pseudomonas aeruginosa* and *Escherichia coli*) and Gram positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*). The methanol extracts followed by acetone extracts of all variety showed more potent inhibitory activity than the diethyl ether and chloroform extracts. However the leaf methanolic extract from the white flowered variety showed highest antibacterial activity at 500 mg/ml followed by the methanolic leaf extracts from pink flowered variety, yellow and orange flowered variety, respectively [40].

The antimicrobial activities of various extracts of *Mirabilis jalapa* tubers were investigated against Gram-positive (*Bacillus cereus*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Micrococcus luteus* and *Enterococcus faecalis*) and Gram-negative (*Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*) bacteria. Water extract was the most effective with minimum inhibitory concentration of <200µg/ml against *Staphylococcus aureus*, *Micrococcus luteus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Bacillus cereus* and *Enterococcus faecalis*. Only water extract showed antifungal activity against *Aspergillus niger*, *Fusarium solani*, *Fusarium oxysporium* and *Fusarium granularium* [28].

The antimicrobial activity of the ethanol, ethyl acetate, chloroform, formaldehyde and distilled water extracts of *Mirabilis jalapa* leaves was tested against *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis*, *Pseudomonas aeruginosa* and *Candida albicans*. The ethanolic leaf extract showed the most potent activity against *Staphylococcus aureus* (36 mm), *Candida albicans* (29 mm), *Bacillus subtilis* (28 mm), *Pseudomonas aeruginosa* (27 mm) and *Escherichia*

coli (24 mm), followed by water extract against *Bacillus subtilis* and *Staphylococcus aureus* (19 and 16 mm, respectively); formaldehyde extracts against *Escherichia coli* (19 mm); and chloroform extract against *Pseudomonas aeruginosa* (18 mm) and *Candida albicans* (14 mm) [41].

The petroleum ether, benzene, chloroform, ethyl alcohol and methanol extracts of the leaves of *Mirabilis jalapa* were examined for antibacterial effect against Gram positive (*Staphylococcus aureus*, *Staphylococcus epidermidis* and *Bacillus subtilis*), Gram negative (*Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella pneumonia*) and antifungal potential against *Candida albicans*. All extracts except petroleum ether extract possessed potent antibacterial and antifungal effects. Methanol extract showed stronger and broader spectrum of microbial activity as compared to other extracts with zones of growth inhibition of 25, 22, 21, 21, 20, 22, 23mm against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Escherichia coli* and *Candida albicans* respectively [42].

The aqueous and ethanolic extract of the leaves of white flowered *Mirabilis jalapa* was screened for antibacterial activities against *Staphylococcus aureus*, *Salmonella typhi*, *Escherichia coli*, *Vibrio cholerae* and *Bacillus subtilis*. The ethanolic extract showed highest (with the reference to the activities of tetracycline which was taken as a standard 100%) inhibition against *Salmonella typhi* (54.74%) than *Staphylococcus aureus* (54%), *Vibrio cholerae* (51.95%), *Escherichia coli* (51.08) and *Bacillus subtilis* (50%), while, the aqueous extracts didn't possess antibacterial activity [43].

The antibacterial effect of the ethanolic leaf extract of *Mirabilis jalapa* was examined against *Salmonella typhi* and *Bacillus cereus*. Zones of growth inhibition for the extract at a concentration of 20 µg/l were 34.33±1.70mm and 51.33±1.88mm against *Salmonella typhi* and *Bacillus cereus*, respectively while the zones of growth inhibition of separated bioactive fraction at 3mg/ml were 40.33±1.33mm and 40.67±1.70mm, against the same microorganisms, respectively [44].

Aqueous, acetone and ethanol extracts of leaves of *Mirabilis jalapa* were tested for antimicrobial activity *in vitro* against biofilm and extended spectrum of beta lactamase (ESBL) producing uropathogenic *Escherichia coli* (UPEC). Ethanol extract of *Mirabilis jalapa* leaves exhibited the most potent antibacterial activity against all tested biofilm producing UPEC strains, whereas it inhibited only the ESBL producing 2 of 4 UPEC strains [45].

Antibacterial activity of the acetone, ethyl acetate, petroleum ether and ethanol extracts of leaves of *Mirabilis jalapa* were tested against biofilm producing uropathogenic *E. coli* (UPEC 1, UPEC17, UPEC 57 and UPEC 82). The acetone extract exhibited a zone of inhibition of 22, 20 and 17 mm respectively against biofilm producing (UPEC 1, UPEC 17 and UPEC 82) strains. The petroleum ether extract exerted a zone of growth inhibition of 18 and 15 mm respectively against biofilm producing strains UPEC 1 and UPEC 17. The ethyl acetate extract exhibited a zone of inhibition of 20, 19 and 21 mm respectively against biofilm producing strains UPEC 1, UPEC 17 and UPEC 82 [13].

Two fractions of the crude extract of from *Mirabilis jalapa* radix (triterpenoid and flavone) showed antimicrobial activity when tested against *Staphylococcus aureus* and *Candida albicans* [46].

A protein isolated from the root and leaf of *Mirabilis jalapa* showed anti-plant viral activity (potato virus X, potato virus Y, potato leaf roll virus, and potato spindle tuber viroid) comparable to that of the roots and leaves of the original plant [47-51].

The purified protein has been shown to inhibit the mechanical transmission of tomato mosaic virus (TMV) in tobacco, tomato, and pepper plants, and cucumber green mottle mosaic virus in cucumber plants [52].

1,2,3,4-tetrahydro-1-methylisoquinoline-7,8-diol compound, isolated from the root of *Mirabilis jalapa* showed a 48% inhibition against HIV-1 reverse transcriptase at 210 µg/ml [30].

The isoflavone and dehydrorotenoid identified in the plant cell culture of *Mirabilis jalapa* possessed antifungal activity with IC₅₀ of 25 and 48 microg/ml, respectively, against *Candida albicans* DSY1024 [53].

2.2. Antiparasitic effect

The anthelmintic activity of aerial parts extracts (20%, 40%, 60%, 80%) of *Mirabilis jalapa* was studied using *Pheretima posthuma* as a test worms. The methanolic extract of *Mirabilis jalapa* caused paralysis in 12.6 min and death in 13.5 min. Albendazole showed the same effect (at 2.3 min and 3.24 min), respectively [54].

The larvicidal activity of crude chloroform, benzene, methanol and ethyl acetate leaf extracts of *Mirabilis jalapa* was investigated against the larvae of three important vector mosquitoes (*An. stephensi*, *Ae. aegypti* and *Cx. Quinquefasciatus*). The highest larvicidal activity was possessed by the leaf methanol extract of *Mirabilis jalapa* against *Cx. Quinquefasciatus*, *Ae. aegypti* and *An. stephensi*, with LC₅₀ of 84.53, 64.58, 57.55 ppm and LC₉₀ values of 159.25, 120.28 and 104.20 ppm, respectively. The mortality rate was positively correlated with concentration [55].

2.3. Antioxidant effect

The total antioxidant capacity of the acetone, ethyl acetate, petroleum ether and ethanol extracts of leaves of *Mirabilis jalapa* was measured by the ferric reducing antioxidant power (FRAP) assay. Ethanolic extract showed more antioxidant potential compared to other extracts [13]. DPPH test was used to determine the antioxidant activity of petroleum ether, chloroform and methanol extracts of both the leaves and bark of *Mirabilis jalapa*. The methanol extract of the plant bark showed antioxidant activity with IC₅₀ value of 598.02 µg/ml compared to ascorbic acid (IC₅₀ 70.985 µg/ml) [56]. Two fractions of the crude extract of *Mirabilis jalapa* radix (triterpenoid and flavone) showed free-radical scavenging activity by using 2,2-diphenyl-1-picrylhydrazyl solution [46].

The antioxidant effect of the methanolic extract of *Mirabilis jalapa* aerial parts was evaluated using hydrogen peroxide scavenging method and reducing power assay method. The methanolic extract of *Mirabilis jalapa* was found to show significant reductive property. *Mirabilis jalapa* extract also caused a moderate dose-dependent inhibition of hydrogen peroxide [57].

The antioxidant activities of various solvent extracts of *Mirabilis jalapa* tubers were investigated using DPPH and lipid peroxidation assay. The water extract was the most potent antioxidant in all models, followed by methanol extract [58].

The antioxidant potential of aerial (bark and leaves) and the root extracts of *Mirabilis jalapa* was investigated using ABTS and DPPH assay methods. In DPPH radical scavenging assay, methanolic root extract at the concentration of 500 µg/ml exhibited 17.53605 ± 0.1071422% inhibition (ED₅₀: 679 µg/ml), while, the methanolic extract of the aerial parts at the concentration of 500 µg/ml exhibited 17.20884 ± 0.08971401% inhibition (ED₅₀: 3723 µg/ml). In ABTS free radical scavenging model, the EC₅₀ values were 1249 µg/ml, 974 µg/ml, 70.28 µg/ml respectively for methanol root and aerial extracts and quercetin respectively [59].

The ethyl acetate extract of the seed epicarp exhibited high free radical scavenging rate as IC₅₀ (DPPH and OH assays) were 6.62 and 3.49 mg dry powder weight /ml [35].

2.4. Dermatological effect

The effects of hydromethanolic extract of tuberous root of *Mirabilis jalapa* and its terpenoid and flavonoid fractions on skin wound healing were studied using excision wound model on rat. The results indicated that flavonoid caused significant decrease (P<0.05) in antioxidant enzyme level as compared to control in wound healing process, whereas terpenoid fraction caused significant increase (P<0.05) in expression of growth factor levels but regeneration and remodeling stages were delayed due to formation of thicker ulcer layer and also there were no hair follicle-like blood capillaries formation which ultimately may lead to formation of hypertrophic scar of wound. The authors concluded that terpenoid fraction prolonged proliferation phase and have tendency to convert the wound into hypertrophic wound [60].

The wound healing activity of the ethanolic extract of the leaves of *Mirabilis jalapa* (1000mg/kg bw) was investigated using excision wound model, incision wound model and dead space wound models in experimentally induced diabetic rats. *Mirabilis jalapa* extract showed significant wound contraction from 9th to 18th day, significantly increase in wound breaking strength, significantly increase in dry tissue weight, and increased hydroxyproline content compared to normal control and diabetic control animals [61].

2.5. Anticancer effect

Brine shrimp lethality bioassay technique was applied to determine the cytotoxic property of petroleum ether, chloroform and methanol extracts of both the leaves and bark of *Mirabilis jalapa*. The petroleum ether extract of the bark showed significant cytotoxic activity with LC₅₀ value of 8.12 µg/ml compared to vincristine sulphate (LC₅₀ value: 0.33 µg/ml) [56].

Mirabilis jalapa protein was tested for anticancer effect against different cell lines. It showed cytotoxicity against T47D and SiHa cell lines while it was relatively less cytotoxic to mononuclear cell. It showed more specific cytotoxic activity

against cancer cell line such as MACF-7, A549, HCT 116, than the normal cell line (Vero). Furthermore it possessed strong apoptotic effects [62-65].

Ribosome-inactivating protein, isolated from the leaves of *Mirabilis jalapa* was more cytotoxic to HeLa cell-line (LC₅₀ 0.65mg/ml) than to Raji cell-line (1.815mg/ml) after 48 hours' incubation time [66].

A protein fraction with properties like ribosome-inactivating protein (RIP) isolated from the leaves of *Mirabilis jalapa* possessed cytotoxic effect against T47D and SiHa cell line. The LC₅₀ against T47D cell line and SiHa cell line were 0.36µg/ml and 5.6µg/ml, respectively. While, it was non toxic against normal cells (LC₅₀ of 21.04µg/ml). It produced more cytotoxic activity toward breast and cervical cancer cells (58-fold and 4-fold, respectively) as compared to normal mononuclear cells [67].

2.6. Antiinflammatory effect

The total alcoholic extract (300 mg/kg) and petroleum ether fractions (200 mg/kg) of leaves of *Mirabilis jalapa* were screened for its anti-inflammatory activity using carrageenan induced rat paw edema and cotton pellet induced granuloma models. The total alcoholic extract and petroleum ether fraction possessed significant anti-inflammatory activity (P<0.01). They also inhibited granuloma formation significantly (P<0.05) in cotton pellet granuloma model, they inhibited the increase in number of fibroblasts and synthesis of collagen and mucopolysaccharides during granuloma tissue formation [68].

The anti-inflammatory activity of aqueous leaves extract of *Mirabilis jalapa* was evaluated using carrageenan and formalin-induced paw edema models in rats. The extract possessed dose dependent anti-inflammatory activity in carrageenan-induced paw edema model, it showed significant (P<0.05) inhibition of paw oedema, 37.5% and 54.0% on 4th hour at the doses of 200 and 400 mg/kg, respectively. In formalin-induced paw edema model, the maximum percentage inhibition in paw edema was 32.9% and 43.0% on 4th day at the doses of 200 and 400 mg/kg, respectively [69].

The anti-inflammatory effect of *Mirabilis jalapa* hydro ethanolic flowers extract was investigated in formaldehyde and Complete Freund's adjuvant (CFA) induced arthritis in rats. The extract significantly suppressed the paw edema in both formaldehyde and CFA models (P<0.001). Body weight, haematological and antioxidant changes in the CFA rats were restored to normal [70].

2.7. Analgesic effect

The antinociceptive effect of leaf ethyl acetate fraction from *Mirabilis jalapa* (10mg/kg, orally) was investigated in mice. The extract fraction caused marked reduction in the pain caused by complete Freund's Adjuvant-CFA, surgical incision and partial sciatic nerve ligation. However, the fraction did not alter the paw edema or the increase in the IL-1β levels produced by CFA. The antinociceptive effect of the fraction was reversed by the pre-treatment of animals with the muscarinic receptor antagonists (atropine, 5mg/kg, sc) or nicotinic receptor antagonists (mecamylamine, 0.001mg/kg, sc.). The fraction did not alter *in vitro* acetylcholinesterase activity in blood or spinal cord samples, but it reversed the increase in the acetylcholinesterase activity observed in the spinal cord samples from mice injected with CFA. Furthermore, the fraction did not alter the indicators of liver or kidney lesion [71].

The antinociceptive effect of *Mirabilis jalapa* crude hydroethanolic leaves and stems extracts was investigated in pain models in mice. The crude hydroethanolic extract of leaves was more potent than the crude extract of stems to inhibit abdominal constrictions induced by acetic acid (ID₅₀ values of 5.5 (2.3-13.1) and 18.0 (11.3-28.5) mg/kg, respectively]. Crude hydroethanolic leaves extract also possessed antinociceptive effect in the tail-flick test. Pre-treatment with naloxone did not modify the antinociceptive effect, but co-administration with atropine completely prevented it, which indicated that the antinociceptive effect might depend on the cholinergic system [72].

2.8. Antidiabetic effect

The hypoglycemic and hypolipidemic activities of ethanolic extract of *Mirabilis jalapa* root were studied in normal and streptozotocin induced diabetic mice (2, 4, 8 g/kg, for 14 before and 28 days after induction). Both after and before induction of diabetes, the repeated administration of 4, 8 g/kg of the extract lowered blood glucose level, improved insulin sensitivity index, lowered serum total cholesterol, triglyceride levels, and decreased triglyceride and increased glycogen content in liver and skeletal muscle. Single administration of the extract (4 and 8 g/kg) possessed hypoglycemic effect in oral glucose tolerance test in normal and diabetic mice, but showed no hypoglycemic and hypolipidemic effects on normal and diabetic mice [73].

The anti-hyperglycemic effect of hydroethanolic leaf extract of *Mirabilis jalapa* was investigated in streptozotocin induced diabetic rats. The hydroethanolic leaf extract at the concentration of 200 and 400 mg/kg showed significant decrease in the levels of glucose, urea, creatinine, aspartate transaminase, alanine transaminase and alkaline Phosphatase in streptozotocin induced diabetic rats [74].

2.9. Antihistaminic and immune-modulatory effects

The antihistaminic activity of an ethanol: acetone (1:1) extract of the roots of *Mirabilis jalapa* was studied using Guinea pig tracheal chain preparation and clonidine-induced mast cell granulation in mice. The extract (0.5 ml of 100 mg/ml) inhibited histamine-induced Guinea pig tracheal chain contractions non-competitively. The extract (100 or 200 mg/kg, ip) also inhibited milk-induced eosinophilia, albumin-induced paw oedema and protected mast cells against clonidine-induced granulation [75].

The immunomodulatory activity of the methanolic extract (100, 200 and 400 mg/kg) of *Mirabilis jalapa* tuber was investigated in mice by using hemagglutination antibody titer, delayed type hypersensitivity, neutrophil adhesion test and carbon clearance test. Oral administration of 200 and 400mg/kg of the methanolic extract of *Mirabilis jalapa* significantly increased antibody titer, phagocytic index, adhesion of neutrophils and positive hypersensitivity response in mice compared to control group [20].

2.10. Antispasmodic effect

The extract of the flowers of *Mirabilis jalapa* (1-1000 µg/ml) exhibited an inhibitory effect (IC₅₀ 18±0.7 µg/ml) on gut smooth muscle contractility, whereas it stimulated the contraction of rabbit aortic muscle (EC₅₀ 11.60±0.26 µg/ml) in a concentration-dependent manner [76].

2.11. Other effects

The aqueous and alcoholic *Mirabilis jalapa* leaves extracts were examined for their inhibitory effects on hyaluronidase. The percentage of inhibition for aqueous extract was 7.5% , and for alcoholic extract was 6.25% with respect to control assays [18].

3. Conclusion

Mirabilis jalapa contained many bioactive metabolites. It possessed wide range of pharmacological and therapeutic effects included antimicrobial, antiparasitic, dermatological, anticancer, anti-inflammatory, analgesic, antidiabetic, antihistaminic, immune-modulatory, antispasmodic and many other pharmacological effects. The current review highlighted the chemical constituents, traditional uses and pharmacological effects of *Mirabilis jalapa*.

Compliance with ethical standards

Acknowledgments

We acknowledged the dean of Thi qar college of medicine and the dean of Thi qar college of pharmacy for the scientific support.

Disclosure of conflict of interest

The authors confirm that this paper's content has no conflict of interests.

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