Chemical constituents and pharmacological effects of *Cynodon dactylon-* A Review

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Abstract: The phytochemical analysis showed that *Cynodon dactylon* contained flavanoids, alkaloids, glycosides, terpenoides, triterpenoids steroids, saponins, tannins, resins, phytosterols, reducing sugars, carbohydrates, proteins, volatile oils and fixed oils. Previous studies showed that *Cynodon dactylon* possessed central nervous, cardiovascular, antidiabetic, gastrointestinal, antioxidant, immunological, antiallergic, antiinflammatory, antipyretic, analgesic, anticancer, dermatological, diuretic, protective, antimicrobial, antiparasitic, insecticidal and repellent. This review will highlight the chemical constituents, pharmacological and therapeutic effects of *Cynodon dactylon*.

Keywords:- pharmacology, pharmacognosy, medicinal plants, constituents, Cynodon dactylon

I. INTRODUCTION

During the last few decades there has been an increasing interest in the study of medicinal plants and their traditional use in different parts of the world [1]. There are hundreds of significant drugs and biologically active compounds developed from the traditional medicinal plants. Plant showed wide range of pharmacological activities including antimicrobial, antioxidant, anticancer, hypolipidemic, cardiovascular, central nervous, respiratory, immunological, anti-inflammatory, analgesic antipyretic and many other pharmacological effects [2-44]. The phytochemical analysis showed that *Cynodon dactylon* contained flavanoids, alkaloids, glycosides, terpenoides, triterpenoids steroids, saponins, tannins, resins, phytosterols, reducing sugars, carbohydrates, proteins, volatile oils and fixed oils. Previous studies showed that *Cynodon dactylon* possessed central nervous, cardiovascular, antidiabetic, gastrointestinal, antioxidant, immunological, antiallergic, antiinflammatory, antipyretic, analgesic, anticancer, dermatological, diuretic, protective, antimicrobial, antiparasitic, insecticidal and repellent. This review will highlight the chemical constituents, pharmacological and therapeutic effects of *Cynodon dactylon*.

II. SYNONYMS

Cynodon dactylon (L.) Pers., Cynodon dactylon var. affinis (Caro & E. A. Sánchez) Romero Zarco, Cynodon dactylon subsp. arcuatus (J. Presl) Kern & Henty, Cynodon dactylon var. arcuatus (J. Presl) J. Kern ex Henty, Cynodon dactylon var. aridus J. R. Harlan & de Wet, Cynodon dactylon var. biflorus Merino, Cynodon dactylon var. coursii (A. Camus) J. R. Harlan & de Wet, Cynodon dactylon var. dactylon, Cynodon dactylon var. densus Hurcombe, Cynodon dactylon var. elegans Rendle, Cynodon dactylon subsp. glabratus (Steud.) A. Chev., Cynodon dactylon var. glabratus (Steud.) Chiov., Cynodon dactylon var. hirsutissimus (Litard. & Maire) Maire, Cynodon dactylon var. intermedius (Rang. & Tadul.) C. E. C. Fisch., Cynodon dactylon var. longiglumis Caro & E. A. Sánchez, Cynodon dactylon f. major (Beck) Soó, Cynodon dactylon var. maritimus (Kunth) Hack., Cynodon dactylon subsp. nipponicus (Ohwi) T. Koyama, Cynodon dactylon var. nipponicus Ohwi, Cynodon dactylon var. parviglumis (Ohwi) Fosberg & Sachet, Cynodon dactylon var. pilosus Caro & E. A. Sánchez, Cynodon dactylon var. polevansii (Stent) J. R. Harlan & de Wet, Cynodon dactylon var. pulchellus Benth, Cynodon dactylon var. sarmentosus Parodi,Cynodon dactylon var. sarmentosus Pers., Cynodon dactylon var. septentrionalis (Asch. & Graebn.) Ravarut, Cynodon dactylon var. stellatus (Willd.) T. Durand & Schinz, Cynodon dactylon f. villosus (Grossh.) Regel ex Roshev., Cynodon dactylon var. villosus Regel, Cynodon dactylon var. villosus Grossh., and Cynodon dactylon f. viviparus Beetle [45].

III. TAXONOMICAL CLASSIFICATION:

Kingdom: Plantae, Subkingdom: Tracheobionta, Super division: Spermatophyta, Division: Magneliophyta, Class: Liliopsida, Subclass: Commelinidae, Order: Cyperales, Family: Poaceae, Genus: Cynodon, Species: Cynodon dactylon [46].

IV. COMMON NAMES

Afrikaans: Gewonekweek, Kweekgras; Arabic: Thaiel, Najeel, Echrish, Tohma; Chinese: Gou ya gen; English: Bahama grass, Bermuda grass, Common couch, Devil's grass, Giant Bermuda grass, Green couch, Hariali grass, Indian couch, Plain couch, Quick grass; French: Chiendent pied-de-poule, Cynodon dactyle,

Grand chiendent; German: Bermudagras, Hundezahngras; India: Dhub, Doob; Italian: Gramina; Portuguese: Capim-Bermuda; Spanish: Grama rastrera, Zacate de Bermuda; Swedish: Hundtandsgräs[47].

V. **DISTRIBUTION**

Probably native to East Africa where it is widely distributed from sea level to 2,160 m altitude. It was now distributed throughout the world in temperate and subtropical regions. In temperate zones, it grew along sea coasts; in tropics, most commonly in areas with 670-1750 mm rainfall; in arid zones. along rivers and on irrigated land[48].

VI. DESCRIPTION

Perennial grass, very variable, with long rapid-growing, creeping runner or stolons, rooting at nodes, forming a dense tuft on the surface of the soil, runners sometimes 20 m long; leaves 2.5-20 cm long, 2-6 mm broad, flat or sometimes folded or convolute; inflorescence on culms 15 cm to 1 m tall consisting of 2-12 spikes arranged star-like at apex of stem; spikes 2.5-10 cm long with numerous spikelets, arranged in 2 rows on one side of spike; spikelets flat, 2-2.5 mm long, awnless, with 1 floret; glumes unequal, the upper longer and one-third to three-fourths length of floret[49].

VII.

TRADITIONAL USES

Traditionally, the plant was used for the treatment of diarrhea, dysentery, wounds, hemorrhages and hyperdypsia. Fresh juice of plant was used as demulcent, astringent and in the treatment of dropsy, anasarca, catarrhal opthalmia, secondary syphilis, chronic diarrhea and dysentery. The fresh expressed juice of the grass was used in hemuturesis, vomiting and as application in catarrhal opthalmia, and also can be applied to cuts and wounds, and in chronic diarrhea and dysentery. Decoctions of root were used in vesical calculus and secondary syphilis, stoppage of bleeding from piles, and irritation of urinary organs [49-53].

Physiochemical analysis of powdered Cynodon dactylon:

Extractive value (water: 18.88, alcohol: 8%, petroleum ether: 3% and benzene: 1.34% w/w of crude drug). Total ash: 9.1 %, acid insoluble ash: 3.7 %, water insoluble ash: 7.9 %, moisture content: 15 %, volatile oil: 1 %, fiber content: 30.46 % and tannin content: 0.80 % [54].

VIII. CHEMICAL CONSTITUENTS

The phytochemical analysis showed that the plant contained flavanoids, alkaloids, glycosides, terpenoides, triterpenoids steroids, saponins, tannins, resins, phytosterols, reducing sugars, carbohydrates, proteins, volatile oils and fixed oils [55-59].

Quantitative estimation of phytoconstituents showed glycosides reached 12.2 %, tannins 6.3%, alkaloids 0.1%, resins 1.0%, free reducing sugar 10% and total reducing sugar 12% [53].

Nutritional analysis showed that each 100 g contained (on a zero-moisture basis) 11.6 g protein, 2.1 g fat, 75.9 g total carbohydrate, 25.9 g fiber, 10.4 g ash, 530 mg Ca, 220 mg P, 112.0 mg Fe, 1630 mg K, 28 µg betacarotene equivalent[60].A total of 20 compounds were identified from the hydroalcoholic extract of the whole parts of Cynodon dactylon. Hexadecanoic acid, ethyl ester linolenic acid, ethy ester d-mannose were the major components of the hydroalcoholic extract, and hexadecanoic acid ethyl ester was the most abundant one (17.49%). However, the isolated compounds were included: 3H-pyrazol-3-one, 2,4-dihydro-2,4,5-trimethyl 2.2112%, 4H-pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl3.2157%, menthol 1.1807%, benzoic acid, 2hydroxy-, methyl ester 2.0455%, benzofuran, 2,3-dihydro 0.9639%, 2-furancarboxaldehvde. 5-(hydroxymethyl)- 2.3088%, 2-methoxy-4-vinylphenol 3.2348%, decanoic acid, ethyl ester 2.4063%, d-3-Tert-butyl-4-hydroxyanisole 0.9040%, Ar-tumerone 5.7431%, tumerone1.9123%, mannose 11.4820%, curlone 4.2422%, tricyclo[6.3.0.0(1,5)]undec-2-en-4-one, 2,3,5,9- tetramethyl 2.89 14%, 3,7,11.15-Tetramethyl-2-hexadecen-1-ol 10.3540%, hexadecanoic acid ethyl ester 17.4905%, phytol 5.2078%, 9.12octadecadienoic acid ethyl ester 6.9257%, linolenic acid ethyl ester 11.2885% and octadecanoic acid ethyl ester 3.9916%. On the other hand, 22 compounds were identified from the phenolic fraction of the whole parts of Cynodon dactylon. Hydroquinone was the most abundant one (69.49%). The isolated compounds were included: propanoic acid, 2-oxo 1.5939%, furfural 6.0224%, 2H-pyran-2-one, 5,6-dihydro 1.3323%, pantolactone 0.8977%, pentanoic acid, 4-oxo 0.7289%, levoglucosenone 2.7253%, hexanediamide, N,N'-dibenzoyloxy 0.9019%, 3-hydroxy-1-methylpyridinium hydroxide 1.4121%, 2-furancarbox-aldehyde, 5- methyl 1.5718%, propanedioic acid, phenyl1.8379%, hydroquinone 69.4771%, phthalic anhydride 1.3128%, 1,3-benzenediol, 5-chloro 1.1284%, benzaldehyde, 3-(chloroacetoxy)- 4-methoxy 0.8016%, ethanone, 1-(4-hydroxy-3methoxyphenyl)- 0.5183%, 1,6-anhydro-á-D-glucopyranose (levoglucosan) 1.0982%, vanillic acid 1.2001%, 1-(2-Hydroxy-4,5-dimethoxyphenyl)-ethanone 0.3610%, Syringic acid 1.1154%, pyrrolidin-2-one, N-(2,4dimethylcyclopent-3-enoyl)-, cis 1.8603%, cinnamic acid, 4-hydroxy-3- methoxy 1.2345% and 9,9-Dimethoxy-bicyclo [3.3.1]nona- 2,4-dione 0.8679% [61].

However, Chandel and Kumar isolated 24 compounds from *Cynodon dactylon* leaves using GC-MS analysis, these included: glycerin 38.49%, 4H-pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl- 2.16%, thymol 1.15%, conhydrin 0.79%, 1,2-cyclopentanediol, 3-methyl- 1.65%, benzenepropanol, 4-hydroxy-à-methyl-, (R)- 0.36%, ethyl à-d-glucopyranoside 8.42%, 3,7,11,15-tetramethyl-2-hexadecen-1-ol 2.01%, n-hexadecanoic acid1.01%, hexadecanoic acid, ethyl ester 9.50%, phytol 4.89%, linoleic acid ethyl ester 5.32%, 9,12-octadecadienoyl chloride, (Z,Z)- 15.61%, octadecanoic acid, ethyl ester 0.72%, pentanal, 2-methyl- 0.58%, 1-(cyclopropyl-nitro-methyl)-cyclopentanol 0.29%, 2-propenamide, N-[2-(dimethylamino)ethyl]- 0.36%, hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl) ethyl ester 0.43%, didodecyl phthalate 0.29%, 13-tetradece-11-yn-1-ol 1.01%, 10-undecyn-1-ol 0.43%, Squalene 1.94%, 9,12-octadecadienoic acid (Z,Z)-, phenylmethyl ester 1.15% and diazoprogesterone 1.44%[62]. HPLC–ESI MS have identified the presence of many flavonoids including apigenin, luteolin, 6-C-pentosyl-8-C-hexosyl apigenin and 6-C-hexosyl-8-C-pentosyl luteolin [57].

IX. PHARMACOLOGICAL EFFECTS PHARMACOLOGICAL EFFECTS ON CENTRAL NERVOUS EFFECT

The ethanol extract of aerial parts of *Cynodon dactylon* showed marked protection against convulsions induced by chemo convulsive agents in mice. The catecholamines contains were significantly increased in the brains of extract treated mice. The amount of GABA, which was most likely to be involved in seizure activity, was increased significantly in mice brain after six week treatment. Results revealed that the extract showed a significant anticonvulsive property by altering the level of catecholamine and brain amino acids in mice[63]. The ethanol extract of aerial parts of *Cynodon dactylon* inhibited the onset and the incidence of convulsion in a

dose dependent manner against pentylenetetrazole-induced convulsion [64].

Anticonvulsant activity of ethanolic extract of *Cynodon dactylon* was studied against maximal electroshock and Pentylenetetrazol (PTZ) induced convulsions in mice. The extract (200, 400, 600 mg/kg) suppressed hind limb tonic extensions induced by MES and also exhibited protective effect in PTZ-induced seizures [65].

The dried extracts of aerial parts of *Cynodon dactylon* were evaluated for CNS activities in mice. The ethanol extract of aerial parts of *Cynodon dactylon* (EECD) was found to cause significant depression in general behavioral profiles in mice. EECD also significantly potentiated the sleeping time in mice induced by standard pentobarbitone sodium, diazepam, and meprobamate in a dose dependant manner[64].

The effects of ethanol extract of aerial parts of *Cynodon dactylon* (EECD) were studied to investigate its CNS depressant pharmacological properties in the classical behavioral models (open-field, elevated plus maze-EPM, Rota-rod, and barbiturate-induced sleeping time) in mice. Extract was given in 50% propylene glycol as a solvent, as a single dose of 50, 75 and 100mg/kg ip. No significant effect was evident on motor coordination of the animals in the rotarod test. On EPM, all the doses of EECD caused significant reduction in the time of permanence in the open arms. In addition, EECD increased the immobility time in the forced swimming test and potentiated pentobarbital-induced sleeping time in mice, confirmed a probable sedative and central depressant effect in the animals[66].

ANTIDIABETIC EFFECT:

The antidiabetic effect of ethyl acetate (70%) extract of *Cynodon dactylon* root and stem, was investigated in diabetes induced by a combination of ketamine (60 mg/Kg) and xylazine (10 mg/Kg) in mice, which induced a sustained hyperglycemia. Mice were treated with 50 and 100mg/Kg *Cynodon dactylon* extract. Both dosages of *Cynodon dactylon* extract had significant lowering effect on blood glucose level. The first dose was more effective than the second, and its impact was just like insulin[67].

250, 500 and 1000 mg/kg bw of aqueous extract of *Cynodon dactylon* were evaluated in diabetic rats and the dose of 500 mg/kg orally was the most effective dose. It lowered blood glucose level around 31% after 4 h of administration in normal rats [68-69].

Aqueous and non-polysaccharide fraction of *Cynodon dactylon* exhibited significant antihyperglycaemic activity in diabetic rats and decreased the glucose, cholesterol, triglyceride, high density lipoprotein, low density lipoprotein and urea levels [70].

The the antidiabetic activity of ethanolic extract of *Cynodon dactylon* root stalks was evaluated in streptozotocin induced diabetic rats. The study showed that the anti diabetic activity of ethanolic extract (500mg/kg) of *Cynodon dactylon* root stalks was comparable with the standard drug, tolbutamide [56]. The antidiabetic activity of aqueous *Cynodon dactylon* extracts was evaluated through an extensive in silico docking approach with PPAR γ (Peroxisome Proliferator-Activated Receptor), GLUT-4 (glucose transporter-4) and SGLT2 (sodium glucose co-transporter-2). Interactions of these molecules with Gln 295 and Asp 294 residues of SGLT2 have been shown to compare well with that of the phase III drug, dapagliflozin. These residues have been proven to be responsible for sugar sensing and transport. This work showed that *Cynodon dactylon* extract was a potential SGLT2 inhibitor for diabetic neuropathy [57].

The antidiabetic, antioxidant and hypolipidemic efficacy of *Cynodon dactylon* were studied in alloxan- induced diabetic rats. A significant diminution of fasting blood sugar level with a significant increase in HDL and decrease (p<0.05) in cholesterol, triglyceride, LDL and VLDL were recorded after 15 days of treatment with 450 mg/kg bw *Cynodon dactylon* leaves extract. The investigation also revealed that the activities of AST, ALT, ALP, AP, LDH, and CPK were significantely (p<0.05) decreased in the extract-supplemented group. In the diabetic rats, the significant decrease in protein content and SOD, CAT, GPx, and GSH (p<0.05) activity and increase in LPO in plasma were found to be ameliorated after treatment with the plant extract [71].

The ability of the secondary metabolites of *Cynodon dactylon* to serve as an antagonist to angiotensin II type 1 receptor (AT_1) was studied. Twenty-four compounds were identified as the secondary metabolites of hydroalcoholic extract of *Cynodon dactylon* using the GCMS technique. Sixteen ligands showed effective binding with the target protein; diazoprogesteron, didodecyl phthalate, and 9,12-octadecadienoyl chloride (z, z) and can be considered as compounds that could be used to bind with the active site sequence of AT_1 . The authors concluded, that the metabolites of *Cynodon dactylon* could serve as a natural antagonist to AT_1 that could be used to treat diabetic retinopathy, so, activation of AT_1 expressed on retinal endothelial cells and pericytes has been implicated in contributing to the microvascular abnormalities in diabetic retinopathy [72].

ANTIMICROBIAL EFFECT

The *in vitro* antibacterial evaluation of the leaves extract of *Cynodon dactylon* was carried out against *Escherichia coli, Staphylococcus aureus* and *Streptococcus pyogenes.* 10% concentration of extract was found to be most effective as antibacterial concentration [73].

The aqueous extract of *Cynodon dactylon* (50-400 mg/ml) was used to determine the antimicrobial activity against *Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Proteus mirabilis* and *Candida albicans*. The aqueous extract of *Cynodon dactylon* exerted concentration dependent antimicrobial activity against all the tested microorganisms except *Candida albicans*[74].

The hydroalcoholic extract of *Cynodon dactylon* was investigated for its antibacterial activity against two Gram positive bacteria (*Staphylococcus aureus* and *Staphylococcus albus*) and two gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) using agar well diffusion method (zone of inhibition) and micro-dilution method (minimum inhibitory concentration). Hydroalcoholic extract of *Cynodon dactylon* possessed an effective antibacterial activity, from results of minimum inhibitory concentration, it appeared that all tested bacterial strains were sensitive to *Cynodon dactylon* extract [75].

The antimicrobial activity of *Cynodon dactylon* crude extracts from seven different solvents (acetone, chloroform, diethyl ether, ethanol, ethyl acetate, methanol, and n-pentane) was investigated against some pathogens (*Bacillus cereus, Bacillus subtilis, Escherichia coli, Klebsiella spp., Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus pyogenes,* and *Streptococcus pneumonia*) using disc diffusion method. The antimicrobial study revealed broad spectrum antimicrobial activity for ethanol (7.0–10.0 \pm 0.0–1.0 mm) and ethyl acetate (7.0–12.0 \pm 0.0–1.0 mm) extracts against all of the bacterial pathogens. Both methanol and acetone extracts showed activity against *B. cereus* (8.0 \pm 0.0 mm) and *B. subtilis* (7.0 \pm 0.0 mm), while chloroform extract showed activity against *B. subtilis* (7.0 \pm 0.0 mm) and *S. pyogenes* (8.3 \pm 0.6 mm). activity was observed from n-pentane extraction. Great antimicrobial activity were observed for both ethyl acetate and ethanol extracts with size of inhibition ranging from 8.0 \pm 0.0 mm to 15.7 \pm 0.6 mm for ethyl acetate and 8.0 \pm 0.0 mm to 13.0 \pm 0.0 mm for ethanol extract. No significant antimicrobial activity was observed against *A. niger*[76].

Six different organic solvents were used to extract the bioactive compounds from the leaves of *Cynodon dactylon* to screen the antibacterial activity against bacterial pathogens (*Bacillus subtilis, Streptococcus pyogens, Klebsiella pneumoniae, Staphylococcus aureus, Escherichia coli, Proteus mirabillis* and *Pseudomonas aeruginosa*) by paper disc method. The butanolic extract of *Cynodon dactylon* was the most active against most of the tested organism, followed by ethyl acetate, methanol, petroleum ether and chloroform extract [77].

The antimicrobial activity of ethanol, methanol, acetone, chloroform, hexane and petroleum ether extract of *Cynodon dactylon* was tested against infectious disease causing bacterial pathogens (*E.Coli, Pseudomonas aeruginosa, Staphylococcus aureus* and *Klebsiella pneumonia*) and fungi (*Aspergillus niger, Candida albicans, Candida kefyr* and *Candida tropicalis*) using the agar well diffusion method. It was observed that ethanol, methanol, acetone, chloroform, hexane and petroleum ether showed activity against bacteria and fungi. The ethanol extract of *Cynodon dactylon* showed more activity against *Pseudomonas aeruginosa* (zone of diameter 13.83±0.29mm), *Staphylococcus aureus* (zone of diameter 12.0±0.10mm) and the ethanol extract of *Cynodon dactylon* showed more activity against *Aspergillus niger* (zone of diameter 12.23±0.21mm) and *Candida albicans* (zone of diameter 11.0±0.20mm), when compared to other solvent extracts [78].

The antimicrobial activity of *Cynodon dactylon* crude extract from three different extraction (hot and cold aqueous extraction and methanol extraction) was investigated against some of the Gram positive bacteria

(*Staphylococcus epidermidis* and *Bacillus cereus*) and Gram negative bacteria (*Escherichia coli, Pseudomonas aeroginosa, Salmonella typhi* and *Shigella dysenteriae*) using disc diffusion method. Amoxicillin and Gentamicin were taken as positive control. The aqueous extract of *Cynodon dactylon* had antimicrobial activity against all the test organisms which indicated broad spectrum activity of the extract against both Gram positive and Gram negative bacteria, while, no clear zone formed with methanol extract [79].

The antibacterial activity of the leaf extracts of *Cynodon dactylon* was investigated against pathogenic bacteria (*Bacillus subtilis, Staphylococcus aureus, Escherichia coli Klebsiella pneumonia* and *Pseudomonas aeruginosa*), by *in vitro* agar well diffusion method. The results showed that chloroform *Cynodon dactylon* leaf extracts possessed antibacterial activity against all the tested bacteria. Chloroform extracts of *Cynodon dactylon* at a concentration of 75μ l /ml exhibited relatively higher zone of inhibition compare to 25 and 50μ l/ml. However, the *Bacillus subtilis, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Staphylococcus aureus* were resistant to aqueous leaf extracts of *Cynodon dactylon* [80].

Antiviral activity of a large scale produced plant extract of *Cynodon dactylon* on white spot syndrome virus (WSSV) was studied in black tiger shrimp *Penaeus monodon* by an *in vivo* testing. The plant extract of *Cynodon dactylon* was incorporated with artificial pellet feed at a concentration of 1% or 2%. *Cynodon dactylon* was highly effective in preventing WSSV infection with no mortality [81].

The *in vitro* virustatic and virucidal tests of the crude extract of *Cynodon dactylon* against infection with porcine reproductive and respiratory syndrome virus (PRRSV), were studied. Crude extract of *Cynodon dactylon* was prepared for cytotoxicity on tissue-culture cells that were used to measure virustatic and virucidal activities against PRRSV. Crude extract of *Cynodon dactylon* at 0.78 mg/ml showed no cytotoxicity on the cell line, and at that concentration significantly inhibited replication of PRRSV as early as 24 hours post infection. *Cynodon dactylon* also inactivated PRRSV as determined by immunoperoxidase monolayer assay (IPMA) compared to the control experiments [82].

The luteolin and apigenin rich fraction was obtained from the ethanolic extract of *Cynodon dactylon*, and it was evaluated for cytotoxicity and anti-Chikungunya potential using Vero cells. The fraction exhibited potent viral inhibitory activity (about 98%) at the concentration of 50 μ g/ml as observed by reduction in cytopathic effect, and the cytotoxic concentration of the fraction was found to be 250 μ g/ml. RT-PCR analyses indicated that the reduction in viral mRNA synthesis in fraction treated infected cells was much higher than that of viral infected control cells [83].

ANTIPARASITIC INSECTICIDAL AND REPELLENT EFFECTS:

Anthelmintic activity of petroleum ether, methanol, and water extracts of *Cynodon dactylon* was evaluated on adult Indian earthworm *Pheretima posthuma* with the using of albendazole as a standard drug. The aqueous extract of *Cynodon dactylon* exerted anthelmintic activity in comparison with the standard drug [58]. The of mosquito repellents activity of volatile oils of *Cynodon dactylon* was studied against (*A. aegypti*). The distillates of the fruits of *Cynodon dactylon* was effective for 3 hours. The mixture of *C. papaya* and *Cynodon dactylon* was effective for 2.5 hours compared to that of *C. papaya* (2.5 hours) alone or *Cynodon dactylon* (1.5

hours) alone[84].

GASTROINTESTINAL EFFECT:

The effect of 50% ethanolic extract of *Cynodon dactylon* was evaluated in gastro-ulcerogenic potential of indomethacin. 50% ethanolic extract of *Cynodon dactylon* was administered in the dose of 300 and 600 mg/ kg orally 30 minutes prior to ulcer induction in male Sprague-Dawley rats by oral administration of indomethacin. Famotidine was used as a reference standard drug. The antiulcer activity was assessed by determining and comparing the ulcer index in the test drug group with that of the vehicle and standard groups. Both the doses, 300 and 600 mg/ kg of test drug showed a protective effect on indomethacin- induced ulcers with 56.74% and

The gastro-protective effect of *Cynodon dactylon* was studied in alcohol and indomethacin induced gastric mucosal damage. The control group received only ulcerogen, whereas the standard control group and test compound groups were pretreated with ranitidine (25mg/kg) and *Cynodon dactylon* (300 and 450mg/kg of the plant juice powder, intragastrically) respectively, before exposure to ulcerogen. 4 hours after exposure to ulcerogen the rats were sacrificed, stomachs were dissected out and opened. The total number of ulcers, size of each ulcer was noted and ulcer index was calculated.. In alcohol model the rats pretreated with *Cynodon dactylon* showed significant protection as compared to control and ranitidine pretreated groups. However in indomethacin model the rats pretreated with ranitidine gave better protection [86].

The extract of *Cynodon dactylon* was investigated for its anti- ulcer activity against pylorus ligation, aspirin induced and ethanol induced gastric ulcer in rats at 100, 200, 300 mg/kg bw. A significant reduction (p<0.01) in ulcer index was seen in *Cynodon dactylon* extract treated rats of pylorus ligation, aspirin induced and ethanol induced gastric ulcer models. The gastroprotective effect was further confirmed by histopathological examination of rat stomach [87].

Alcoholic extract of *Cynodon dactylon* was evaluated at 200, 400, and 600 mg/kg bw, orally for pylorus ligated and indomethacin induced gastric ulcer models in albino rats. Alcoholic extracts at 400 and 600 mg/kg showed significant (p>0.001) antiulcer activity, comparable to the standard drug ranitidine [88].

The hexane, dichloromethane, ethyl acetate and methanol extracts of *Cynodon dactylon* whole plant were tested for anti-diarrheal activity on castor oil induced diarrhea, gastro intestinal motility by charcoal meal and enteropooling models in albino rats. Methanol extract exhibited considerable inhibition of castor oil induced diarrhea. Methanol extract also showed a significant decrease in gastrointestinal motility by charcoal meal and decrease in weight of intestinal contents in enteropooling models. The results indicated that the plant possessed good anti- diarrheal activity [89].

ANTIOXIDANT EFFECTS:

The effect of ethyl acetate fractions of *Cynodon dactylon* on the level of enzymatic and non enzymatic antioxidants was studied in Ehrlich's lymphoma ascite (ELA) transplanted mice. The levels of enzymatic antioxidants like super oxide dismutase, glutathione peroxidase and catalase and non enzymatic antioxidants like reduced glutathione, vitamin A and vitamin E, were decreased in ELA induced mice due to the liberation of free radicals from the liver. Administration of ethyl acetate extract (80 µg in 100 µl of DMSO, ip) increased levels of enzymatic and non enzymatic antioxidants in ELA transplanted mice [90].

Cynodon dactylon was sequentially extracted with hexane, ethyl acetate, and methanol, then the extracts were concentrated and tested for antioxidant activity using 1,1-diphenyl-2-picrylhydrazyl, nitric oxide and 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide assays on four cancer cell lines and a normal cell line. The anticancer potential of cytotoxic extracts was determined by the Annexin-fluorescein isothiocyanate-conjugated assay in human colon adenocarcinoma cell lines (COLO 320 DM). *Cynodon dactylon* extracts showed significant antioxidant and antiproliferative activities[91].

The antioxidant activity of the hydroalcoholic extract of aerial parts of *Cynodon dactylon* was studied *in vitro* by different methods (DPPH radical scavenging activity, superoxide anion radical scavenging assay, nitric oxide scavenging assay, ferrous chelating ability, hydroxyl radical scavenging assay, hydrogen peroxide scavenging activity and ABTS assay). In all the methods, the extract showed ability to scavenge free radicals in a concentration dependant manner. Superoxide anion radical scavenging assay showed a maximum inhibition of 93.33%. Total antioxidant capacity equivalent of ascorbic acid was 172.39 mg/g of extract [92].

Selected isolates from ethyl acetate extract of *Cynodon dactylon* and piper betle and the combination of both were found to have antioxidant activity. The selected isolates showed better activities in combination rather than individual form[93].

CARDIOVASCULAR effects

Cynodon dactylon caused rise in heart beat rate in zebra fish embryos significantly higher than that caused by betamethosone. The EC_{50} value of *Cynodon dactylon* was found to be 3.738 µg/ml [94].

The effects of hydroalcoholic extract of *Cynodon dactylon* rhizomes was evaluated on cardiac contractility in normal hearts and on cardiac functions in right-heart failure in rats. Right-heart failure was induced by intraperitoneal injection of monocrotaline (50 mg/kg). Two weeks later, the animals were treated orally with different doses of the extract for fifteen days. At the end of the experiments, cardiac functions and markers of myocardial hypertrophy were measured. The treated rats showed very less signs of fatigue, peripheral cyanosis and dyspnea. The survival rate was high in the extract treated groups (90%). Administration of *Cynodon dactylon* in monocrotaline-injected rats led to profound improvement in cardiac functions as demonstrated by decreased right ventricular end diastolic pressure (RVEDP) and elevated mean arterial pressure. RVdP/dtmax, and RVdP/dt/P as indices of myocardial contractility were also markedly (p<0.001) increased by the extract. The extract reduced heart and lung congestion by decreasing tissue wet/dry and wet/body weight ratios (p<0.01). In the isolated rat hearts, the extract produced a remarkable (p<0.001) positive inotropic effect concomitant with a parallel decrease in LVEDP [95].

The phenolic fraction of *Cynodon dactylon* (CDP) was evaluated for its cardio-protective activity using isolated frog's heart perfusion method. The CDP produced negative inotropic and chronotropic actions on isolated frog heart. These pharmacological effect were selectively inhibited by atropine, which indicated that these effects were mediated through muscarinic receptor [96].

The probable antiarrhythmic effects of *Cynodon dactylon* against ischemia/ reperfusion (I/R)-induced arrhythmias were investigated in isolated rat heart. The hearts were subjected to 30min regional ischemia followed by 30min reperfusion and perfused with hydroalcoholic extract of rhizome of *Cynodon dactylon* (25, 50, 100 and 200µg/ml). During ischemia, the extract produced marked reduction in the number, duration and incidences of ventricular tachycardia (VT) at 25 and 50µg/ml (p<0.001 and p<0.01) respectively. Total number of ischemic ventricular ectopic beats (VEBs) were lowered by 25, 50, 100µg/ml (p<0.001, p<0.001 and p<0.050 respectively. At the reperfusion phase, *Cynodon dactylon* (25 and 50µg/ml) decreased incidence of VT from

100% (control) to 13 and 33% (p<0.001 and p<0.05) respectively. Duration and number of VT and total VF incidence were also reduced at the same concentration (p<0.05 for all). Perfusion of the extract (25, 50, 100µg/ml) was markedly lowered reversible VF duration from 218±99second to 0 second, 0 second and 10±5 second (p<0.01, p<0.01 and p<0.05) respectively. Moreover, *Cynodon dactylon* (25 and 50µg/ml) decreased number of total VEBs from 349±73 to 35±17 (p<0.001) and 66±26 (p<0.01). it was also shown that perfusion of the extract produced a marked and concentration-dependent positive inotropic effect [97].

The haemostatic activity of *Cynodon dactylon* was studied in albino rats. The Bleeding Time (BT) in control group was 160.5 ± 8.3 second and in test group 96.8 ± 10.3 second. The Clotting Time (CT) in control group was 507.6 ± 18.2 second and in test group 319.3 ± 27.1 second [98].

IMMUNOLOGICAL AND ANTIALLERGIC EFFECTS:

The possible antianaphylactic and mast cell stabilization mechanism of *Cynodon dactylon* was evaluated by using compound 48/80 induced mast cell activation and level of nitric oxide in serum, rat peritoneal mast cells. The results showed that a *Cynodon dactylon* compound (CDC) isolated by bio-assay guided fractionation, produced significant (p<0.01) inhibitory effect on compound 48/80 induced anaphylactic reaction and (p<0.001) mast cell activation. This CDC also inhibited significantly, compound 48/80 induced increased level of nitric oxide in rat serum and rat peritoneal mast cells [99].

The immunomodulatory activity of *Cynodon dactylon* was carried out in mice using the humoral antibody response. Oral administration of the juice at 250 and 500 mg/kg in mice increased humoral antibody response upon antigen challenge as evidenced by a dose-dependent, significant increase in antibody titer in the haemagglutination antibody assay and plaque forming cell assay [100].

ANTIINFLAMMATORY, ANTIPYRETIC AND ANALGESIC EFFECTS:

The anti-inflammatory activity of aqueous extracts of *Cynodon dactylon* (200, 400, and 600 mg/kg of bw orally) was evaluated using the carrageenan, serotonin dextran and histamine induced rat paw edema. The results showed that all doses exerted significant anti-inflammatory activity in all models [101].

The 50% ethanolic extract of *Cynodon dactylon* at 300 and 600 mg/kg was investigated for possible antiinflammatory and analgesic activity in several rodent model of inflammation and pain, including carrageenaninduced rat paw edema, cotton pellet granuloma method and biochemical parameters (Serum SGOT and SGPT levels) and lipid peroxide formation in experimental inflammation. The results revealed that the extract oral treatment for 7 days in albino rats, was significantly inhibited carrageenan-induced edema. It showed activity against granuloma formation and reduced enzymes activity (SGOT and SGPT), which were elevated in inflammation. The extract also elicited a pronounced inhibitory activity against increased output of peroxides found during the inflammation. Analgesic activity was studied using acetic acid-induced writhing and tail immersion method in albino mice. The extract significantly increased the pain threshold when evaluated for acetic acid induced writhes [102].

The analgesic and anti-pyretic activities of aqueous extract of *Cynodon dactylon* at different doses was studied using hot plate, acetic acid induced writhing and yeast induced hyperthermia in rats. *Cynodon dactylon* showed significant analgesic and anti-pyretic activities in all models studied [103].

The antipyretic effect of aqueous extract of *Cynodon dactylon* was studied in mice, it was found that at the dose of 600 mg/kg, the aqueous extract possessed significant decrease in rectal temperature of mice similar to that shown by paracetamol[103].

A significant increase in the levels of inflammatory mediators, myeloperoxidase, nitrite, C-reactive protein, ceruloplasmin was observed in rats with adjuvant- induced arthritis. This was associated with oxidative stress with a marked reduction in the activity of catalase, superoxide dismutase, glutathione peroxidase and the levels of glutathione, vitamins C and E and an increase in the lipid peroxidation as indicated by the higher levels of thiobarbituric acid reactive substances. *Cynodon dactylon* (20mg/kg/ bw) orally administered to arthritic rats after adjuvant injection produced a significant attenuation in the inflammatory response, oxidative stress and ameliorated the arthritic changes to near normal conditions[104].

The effects of the aqueous extract prepared from the rhizomes of *Cynodon dactylon* was investigated on vascular endothelial growth factor (VEGF) expressions in human umbilical vein endothelial cells (HUVECs) and also on angiogenesis in carrageenan induced air-pouch model in rats. Oral administration of 400 mg/kg/day of the extract significantly increased angiogenesis (p<0.05) and markedly decreased neutrophil (p<0.05) and total leukocyte infiltration (p<0.001) into the granulation tissues. Moreover, the extract increased the expression of total VEGF in HUVECs at a concentration of (100 µl/ml). Accordingly, the aqueous extract of *Cynodon dactylon* promotes angiogenesis probably through stimulating VEGF expression [105].

The ethanol extract of aerial parts of *Cynodon dactylon* significant reduced the number of writhes and stretches induced in mice by 1.2% acetic acid solution. It also potentiated analgesia induced by morphine and pethidine in mice [64].

ANTICANCER EFFECT:

Anticancer activity of *Cynodon dactylon extract* was evaluated in Swiss albino mice after inoculated with Ehrlich ascites carcinoma (EAC) cells. The extract were administered orally as three doses, 100, 200 and 400 mg/kg bw for ten consecutive days. Anticancer activity of the *Cynodon dactylon* extracts was evaluated by mice life span, which increased based on mean survival time (MST)[106].

The anticancer activity of methanolic extracts of leaves of *Cynodon dactylon* was studied in ascitic lymphoma (ELA) in Swiss albino mice. The tumor was induced in mice by intraperitoneal injection of EAC (1×10^6 cells/mouse). The result revealed that methanolic extract of *Cynodon dactylon* possessed significant antitumor and hepatoprotective effect [107].

The antiproliferative, apoptotic and antioxidant potentials of *Cynodon dactylon* were investigated by 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay, nitric oxide radical scavenging activity (NO⁻) and MTT assay on four cancer cell lines (COLO 320 DM, MCH-7, AGS, A549) and a normal cell line (VERO). *In vivo* chemopreventive property of the plant extract was studied in DMH-induced colon carcinogenesis. The methanolic extract of *Cynodon dactylon* was found to be antiproliferative and antioxidative at lower concentrations and induced apoptotic cell death in COLO 320 DM cells. Treatment with methanolic extract of *Cynodon dactylon* also increased the levels of antioxidant enzymes and reduced the number of dysplastic crypts in DMH-induced colon of albino rats [108].

PROTECTIVE EFFECTS

The effect of *Cynodon dactylon* in restoration of the male reproductive dysfunction induced by immobilization stress, was studied by evaluation sexual behavioral, sexual performance, fructose content of the seminal vesicles, epididymal sperm concentration and histopathological examinations. Treatment of rats under stress with methanolic extract of *Cynodon dactylon* has shown a promising effect in overcoming stress-induced sexual dysfunction, sexual performance, fructose content, sperm concentration and its effect on accessory sexual organs and body weight. The authors concluded that *Cynodon dactylon* methanolic extract had a potent aphrodisiac and male fertility activity [109].

The methanolic extract of roots of *Cynodon dactylon* was screened for its hepato-protective activity in diethyl nitrosamine (DEN) induced liver cancer in Swiss albino mice. The plant extract at a dose of 50 mg/kg was administered orally once a week, up to 30 days after DEN administration. Diethyl nitrosamine treated group showed low significant elevation (p<0.05) in liver GST activity with respect to control, whereas the control, DEN + *Cynodon dactylon*, DEN + tamoxifen treated animals did not shown any alteration. A highly significant (p<0.01) elevation in GPx activity was observed in DEN treated mice, whereas DEN + *Cynodon dactylon* showed low significant alteration, while saline and DEN + tamoxifen treated animals did not show any significant alteration. DEN, DEN + *Cynodon dactylon* showed low significant depletion (p<0.05) in liver CAT activity with respect to control, whereas saline and DEN + Tamoxifen treated animals did not showed any significant alteration [110].

The hepatoprotective activity of roots of *Cynodon dactylon* in CCl_4 induced hepatotoxicity was studied in albino rabbits. Alcoholic extracts of roots of *Cynodon dactylon* was administered orally for 20 days in a doses of 100mg/kg/day. *Cynodon dactylon* extract was able to bring down the level of serum transaminase, serum alkaline phosphatase, serum bilirubin and increased in serum albumin significantly (p<0.001), when compared with untreated group [111].

The neuroprotective effects of the aqueous extract of *Cynodon dactylon* (AECD) was investigated in aluminium-induced neurotoxicity in rats. Male albino rats were administered with AlCl₃ at a dose of 4.2 mg/kg/day ip for 4 weeks. Experimental rats were given *Cynodon dactylon* extract in two different doses of 300 mg and 750 mg/kg/day orally 1 h prior to the AlCl₃ administration for 4 weeks. At the end of the experiments, antioxidant status and activities of ATPases in cerebral cortex, hippocampus and cerebellum of rat brain were measured. Aluminium administration significantly decreased the level of GSH and the activities of SOD, GPx, GST, Na⁺/K⁺ ATPase, and Mg²⁺ ATPase and increased the level of lipid peroxidation (LPO) in all the brain regions when compared with control rats. Pre-treatment with AECD at a dose of 750 mg/kg bw increased the antioxidant status and activities of membrane-bound enzymes Na⁺/K⁺ ATPase, and Mg²⁺ ATPase and also decreased the level of LPO significantly, when compared with aluminium-induced neurotoxicity group[112].

The effect of hydroalcoholic extract of *Cynodon dactylon* was evaluated in ethylene glycol-induced nephrolithiasis in a rat model. *Cynodon dactylon* extract reduced the levels of calcium oxalate deposition especially in medullary and papillary sections from of the kidney of the treated rats [113].

The beneficial effect of different fractions of *Cynodon dactylon* was studied in ethylene glycol-induced kidney calculi in rats. Male Wistar rats were randomly divided into control, ethylene glycol, curative, and preventive groups. The control group received tap drinking water for 35 days. Ethylene glycol, curative, and preventive groups received 1% ethylene glycol for induction of calcium oxalate (CaOx) calculus. Preventive and curative

subjects also received different fractions of *Cynodon dactylon* extract in drinking water at 12.8 mg/kg, since day 0 and day 14, respectively. After 35 days, the kidneys were removed and examined for histopathological findings and counting the CaOx deposits in 50 microscopic fields. In curative protocol, treatment of rats with *Cynodon dactylon* n-butanol fraction, significantly reduced the number of the kidney CaOx deposits compared to ethylene glycol group. In preventive protocol, treatment of rats with *Cynodon dactylon* ethyl acetate fraction significantly decreased the number of CaOx deposits compared to ethylene glycol group [114].

DIURETIC EFFECT

The diuretic activity of aqueous extract of *Cynodon dactylon* was evaluated in rats. Aqueous extract of *Cynodon dactylon* at a dose of 100, 250, 500mg, 750 mg/kg bw orally, showed diuretic activity. Rats received aqueous extract at the dose of 750mg/kg/body weight excreted nearly four folds urine as compared to the control group. The excretion of sodium, potassium and chloride ions were also increased [115].

The diuretic potential and effect on urinary electrolytes of aqueous *Cynodon dactylon* L. (Poaceae) rhizomes extract was studied in rats. Different concentrations of plants extract (0.125, 0.250, and 0.500 g/kg of body weight) or the reference drug furosemide (0.015 g/kg) were administrated orally to hydrated male Wistar rats and their urine output was measured at several interval of time after a single dose administration. The results showed that furosemide induced significant diuresis and electrolytes excretion during the first hours. Plant extracts increased significantly urinary output and electrolytes excretion at the dose of 0.500 g/kg. This diuretic effect seems to be not related to K^+ plant content. Urinary pH remained mostly unchanged during the course of the study . No lethality was observed among animals [116].

The diuretic activity of *Cynodon dactylon* was evaluated in rats and in Guinea pigs in comparison with hydrochlorothiazide. Crude extract of plant was administered to rats orally at a dose of 1.25 and 2.5ml/kg. The diuretic activity of extract was evaluated by estimation of urine volume, sodium, potassium and chloride content. The plant administered group showed significant increase in urine output, urinary electrolyte excretion compared to control group. High dose of *Cynodon dactylon* extract group produced results comparable to standard drug [117-118].

DERMATOLOGICAL EFFECT

The wound healing activity of hydroalcoholic extract of *Cynodon dactylon* was evaluated by using excision wound model. The parameters included the rate of wound contraction and the period of epithelization in excision wound model. Herbal ointment was prepared using different bases and concentrations 7.5% and 10% compared with standard cipladine (povidone-iodine). According to the healing parameters, the topical application of hydrochloric extract of *Cynodon dactylon* promoted wound healing activity in excision model in rat[119].

Wound healing potential of *Cynodon dactylon* was evaluated in different experimental model such as excision wound healing model and Incision wound healing model in albino Wistar rats by using the gel preparation of aqueous and alcoholic extract. Alcoholic and aqueous extract gel showed significant increased in the rate of wound healing in excision model (p<0.05) and in excision model (p<0.01)[59].

The wound healing activity of flavonoid fraction of *Cynodon dactylon* was evaluated in excision wound in mice. The flavonoid fraction of *Cynodon dactylon* were applied externally daily on the excised wound area for 8 days. The flavonoid fraction facilitated the healing process as evidenced by increase in collagen and protein and decrease in lipid peroxide in granulation tissue [120].

BRONCHODILATORY EFFECT:

The bronchodilatory effect of *Cynodon dactylon* was investigated by *in vitro* and *in vivo* models. Acetylcholine (Ach)-induced bronchospasm was conducted in guinea pig while isolated rat tracheal strip was suspended in organ bath to measure the concentration response curve using multichannel data acquisition system. The chloroform extract of *Cynodon dactylon* (CECD) protected against Ach-induced bronchospasm in guinea pigs, similar to atropine. In the *in vitro* studies, CECD relaxed carbachol (CCh) and high K⁺ -induced contraction of rat tracheal strip, similar to atropine and verapamil, suggesting antimuscarinic and calcium channel blocking (CCB) activities, which were confirmed by right ward shifting of CCh and Ca⁺² concentration response curve (CRC). The phosphodiestrase (PDE) inhibitory activity was confirmed by potentiation of scopoletin as an active ingredient. It significantly inhibited high K⁺, and Ca⁺² induced contractile response, similar to verapamil. The phosphodiestrase inhibitory activity was confirmed by direct evidence of potentiation of isoprenaline-induced inhibitory response, similar to papaverine. The results revealed that the bronchodilator activity of CECD was partly due to presence of scopoletin, and mediated possibly through CCB and PDE inhibition [121].+

Reproductive effect:

The effect of administration of aqueous extract of entire plant of *Cynodon dactylon* for thirty days on reproductive hormones and reproductive organ weight of female, was studied in Wistar rats. Administration of the extract produced significant increase (p<0.001) in the serum estradiol concentration whereas, follicle stimulating and luteinizing hormones were significantly (p<0.001) reduced. Furthermore, a significant increase (p<0.001) in the weight of the uterus and significant decrease in the weight of the ovaries (p<0.001) was observed in the treated group when compared to the control group. In addition, the estrous cycle was found to be irregular and disturbed [122-123].

Toxicity:

The aqueous extracts of *Cynodon dactylon* was found safe and there was no mortality up to 4000 mg/Kg in rats [124]. Aqueous *Cynodon dactylon* rhizomes extract caused 50% of rat death (LD₅₀) at 4.5 g/kg [116].

X. CONCLUSION

This review discuss the chemical constituent, pharmacological and therapeutic effects of *Cynodon dactylon* as promising herbal drug because of its safety and effectiveness.

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