



A Review on Phytochemicals and Pharmacological Activities of the medicinal plant *Drynaria quercifolia*

Mudavath Ravi Naik ¹, Praveen Thaggikuppe Krishnamurthy^{1*}

¹Department of Pharmacology, JSS College of Pharmacy, JSS Academy of Higher Education and Research, Ooty, The Nilgiris, Tamil Nadu, India.

Corresponding author: Dr. Praveen Thaggikuppe Krishnamurthy

praveentk7812@gmail.com, praveentk@jssuni.edu.in

Abstract

Drynaria quercifolia (DQ) also known as oak leaf plant, is epiphytic therapeutic greenery. The DQ rhizome and leaves are significantly used to promote health. The plant is a member of the polypodiaceae family and is widely used by traditional communities around the world to treat a variety of ailments based on their traditional uses. Phytoconstituents isolated from the plant include friedelin, epifriedelinol, β -sitosterol, β -amyrin, 3,4-dihydroxybenzoic acid, β -sitosterol 3- β -D-glucopyranoside, naringin, naringenin and acetyl lupeol. The plant is used as an analgesic, anti-inflammatory, anti-arthritic, anti-fertility, antimicrobial, anthelmintic, antipyretic, antidiabetic, antihyperlipidemic, thrombolytic, antiurolithiatic, antiulcer, antifungal, antihelmintic, cytotoxic and mosquito repellent. Compounds isolated from the plant that are responsible for the pharmacological activities. So far, the review has provided phytochemical and pharmacological action of the plant.

Key words: *Drynaria quercifolia*, Polypodiaceae, Phytoconstituents, Epiphytic, Oak leaf.1.

Introduction

Natural plants are rich in secondary metabolites and are considered primary sources in medicine, having been used for a long time to treat a variety of diseases. The lead compound isolated from the medicinal plant has more beneficial effects in treating various ailments while having fewer side effects than synthetic chemical compounds. Plants have a high medicinal value in the treatment of life-threatening diseases such as cancer. Plant medicines are used by approximately 80% of global residents to treat routine health problems. Aspirin, atropine, morphine, codeine, taxol, vincristine, quinine, reserpine, colchicine, digitalis, and Physostigmine are examples of modern medicines derived from natural products. Plants contain a high concentration of antioxidants, which inhibit free radicals, causing the disease (Rasool Hassan 2012; Akerele 1993; Lai and Lim, 2011). DQ is an epiphytic fern with a small root system that is attached to its host plant (Figure 1). It is also known as oak leaf fern or basket fern. It is a member of the Pteridophyta family Polypodiaceae. The minerals and

nutrients derived by the epiphytic plant are derived from the external environment as debris accumulated around it (**Vikas et al., 2016**). Pteridophytes comprised 305 genera and over 10,000 species worldwide, with India accounting for around 191 genera and over 1000 species (**Joseph and Thomas, 2015**). DQ mostly distributed in India, Bangladesh, Malaysia, Southeast Asia, New Guinea, Southern China, the Philippines, Pakistan, North America, Sri Lanka, Indonesia, and Australia (**Janarthan et al., 2016; Ranil and Pushpa Kumara, 2008; Sivaraj et al., 2018**). It thrives in open areas and at low elevations (**Neel et al., 2018**). DQ consist of dimorphic fronds (Leaves) which includes sterile nest fronds and fertile foliage fronds. Sterile fronds are small and concave with no sori and that turn brown with age. Fertile foliage fronds are large, pinnatifid and bear sori at the basal surfaces. In between the secondary veins, the sori are either dispersed or aligned in two regular chains. The nest fronds resemble oak leaves, thus the common name (Oak leaf fern) (**Rajesh et al., 2016**). DQR creeping, long, fleshy, up to 2 cm thick, densely clothed with scales and roots (Figure 1) (**Singh**).



Figure 1: (a & b) DQ leaves (c & d) DQ rhizome

Table 1: DQ plant profile

Taxonomy		Vernacular name	
Kingdom	Plantae	English	Oak leaf fern
Division	Pteridophyta	Tamil	Mudavattukal
Class	Polyppodiopsida/pteridopsida	Sanskrit	Aswakatri
Order	Polypodiales	Malayalam	Matipanna, pannakizhangu, pannikizhangu
Family	Polypodiaceae	Kannada	Hanuma hastha, hanuma paada
Subfamily	Polypodiaceae	Hindi	Asvakatri, Katikapan, basingh.
Genus	<i>Drynaria</i>		
Species	<i>Quercifolia</i>		

Table 2: Traditional uses of DQ

Traditional uses	Reference
<ol style="list-style-type: none">1. To reduce Typhoid and hectic fever2. To treat tuberculosis and asthma3. To treat Jaundice4. Relieve head ache5. To reduce throat infection6. To control Phthisis7. Poultice for swelling8. Bowel inflammation9. Skin diseases10. In treatment of Syphilis11. Restore sinews, muscles and bones12. Relieve body pain and knee pain13. Treat intestinal worm and abdominal pain14. Treat urinary problem and spermatorrhoea15. To reduce Rheumatic pain16. To treat Cholera17. Treating Osteodynia and dentagia18. To restore hair growth	<p>Pawar et al., 2017; Sen and Ghosh, 2011; Hedge et al., 2006; Das et al., 2009; Alam 1992; Ueda et al., 2002; Tran et al., 2015</p>

Table 3: The pharmacological activity of DQ

Name of the biological Activity	Preclinical method	Reference	
Cytotoxicity	Brine shrimp lethality bioassay	Khan et al., 2012; Mohanta et al., 2013a	
Antioxidant	DPPH radical scavenging assay	Beknal AK et al.,2010	
	DPPH radical scavenging activity	Jinu et al., 2014	
	Hydroxyl radical scavenging activity		
	Nitric oxide scavenging activity		
	Hydrogen peroxide activity		
	ABTS radical scavenging activity		
	DPPH radical scavenging assay	Amoroso 2017	
	DPPH scavenging activity	Sivaraj et al., 2018	
	ABTS scavenging activity		
	Nitric oxide radical scavenging activity		
	Hydroxyl radical scavenging activity		
	Ferric reducing power activity Phosphomolybdenum reduction assay		
	Reducing power activity.		Das et al., 2014a
	Superoxide anion radical scavenging		
	DPPH free radical scavenging activity		
	DPPH assay	Mohanta et al., 2013a	
	Total antioxidant activity	Prasana and Chitra, 2015b	
	Reducing power assay		
	Nitric oxide scavenging assay		
	Hydrogen peroxide radical		

	scavenging	
Antimicrobial	Agar well diffusion method	Anamika et al., 2015; Prasana et al., 2014.
	Agar well diffusion and disc diffusion method	Padhy and Dash, 2015
	Disc diffusion method	Seena and Valsamma 2018; Khan et al., 2007a; Shokeen et al., 2005; Mithraja et al., 2012; Khan et al., 2012.
	Kirby-Bauer's/disc-diffusion method	Rajesh et al., 2017
Anti-inflammatory	Carrageenan-induced paw oedema	Das et al., 2014a; Janaranjani et al., 2014; Anuja et al., 2014b.
	HRBC membrane stabilization method	Prasana and Chitra, 2015c.
	Histamine-induced paw edema and cotton pellet granuloma formation in rats.	Anuja et al., 2014b.
	Albumin denaturation, membrane stabilization, and COX-1 and COX-2 inhibition assay.	Das et al., 2014a.
Analgesic	Acetic acid writhing inhibition, radiant heat tail-flick	Anuja et al., 2014b; Mohanta et al., 2013b.
	Formalin test in mice, capsaicin-induced paw licking in mice, and hot plate test in mice.	Anuja et al., 2014b.
	Capsaicin-induced nociception, glutamate-induced nociception, tail-flick and tail immersion methods.	Anuja et al., 2014a.
Antidiabetic &	Alpha-amylase inhibition assay and	Prasana et al., 2019.

hypolipidemic	glucose uptake assay	
	Oral glucose tolerance test	Rajimol et al., 2013
Antifibrotic	Cytotoxicity assay (MTT)	Desai et al., 2019
Antipyretic	Yeast induced hyperpyrexia in rats	Janaranjani et al., 2014
Antidematophytic	Agar dilution and disc diffusion methods.	Neja and Deokule; 2009
Antidiarrhoeal	Castor oil-induced diarrhea, GIT motility test, and castor oil-induced enteropooling	Padhy et al., 2016
Hepatoprotective	MTT assay	Devika and Prasana, 2016; Kamboj and Kalia, 2013
Antifertility	Ex-vivo assay for uterine contractile activity, Determination of abortifacient activity. Determination of anti-implantation activity	Das et al., 2014b

2. Phytoconstituents

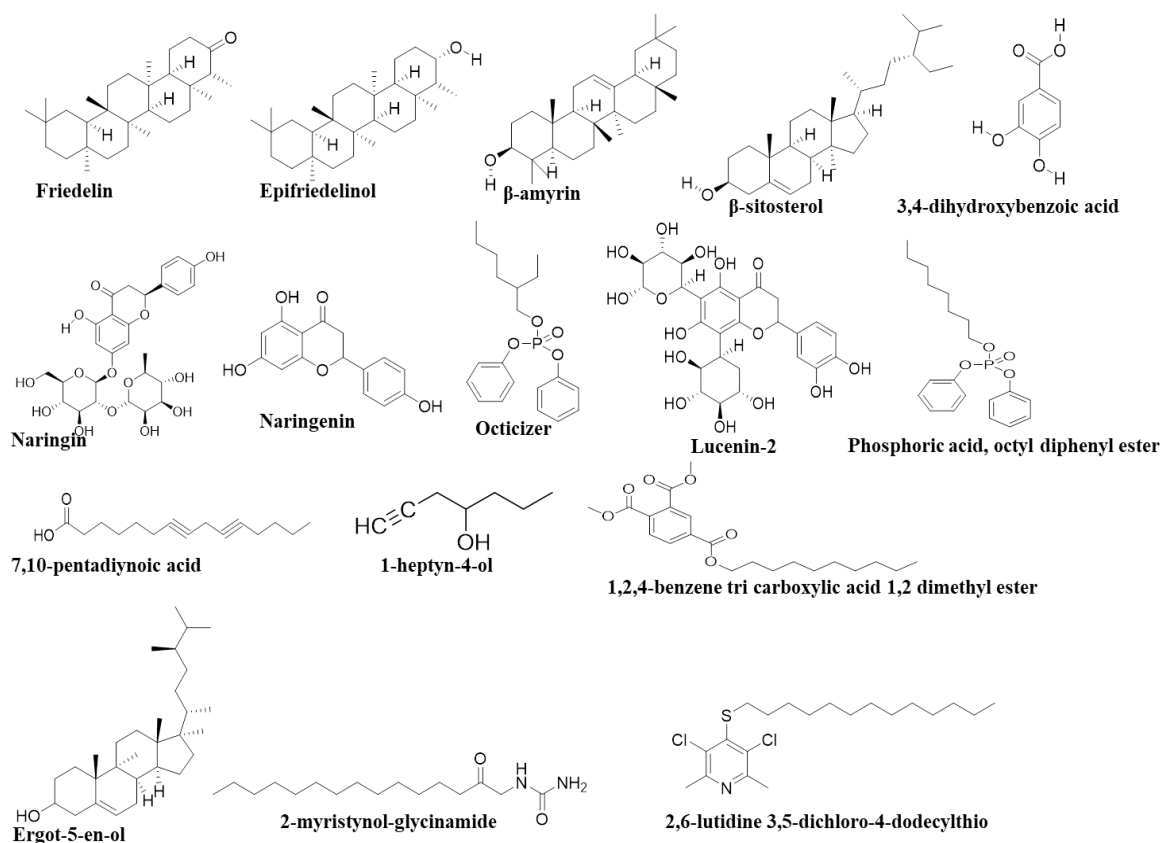


Figure 2

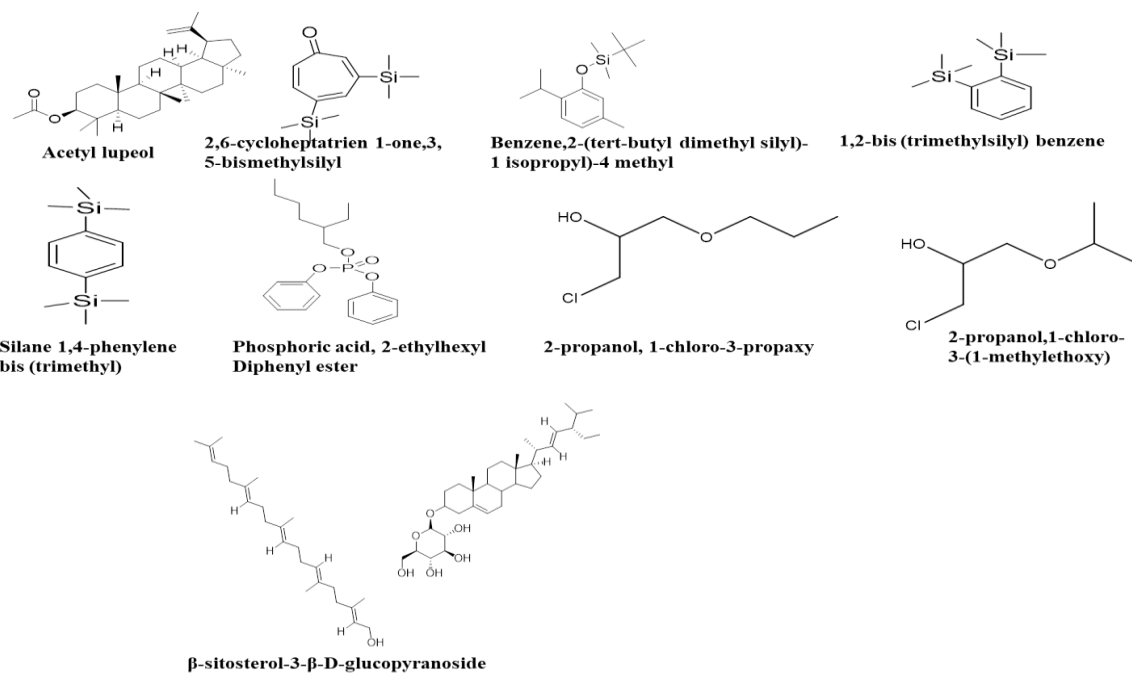


Figure 3

Figure 2 & 3: Reported phytoconstituents of DQ

Phytochemicals such as carbohydrates, saponins, tannins, flavonoids, sterols, terpenoids and proteins and free amino acids were reported in the ethylacetate extract of DQR. HPLC analysis revealed the presence of 1.6% of naringin and 0.15% of naringenin in ethylacetate extract of the DQR (**Anuja et al., 2014a; Janarthan et al., 2016**). Ethanol extract of DQR detected the phytochemicals like carbohydrates, saponins, tannins, flavonoids, proteins and free amino acids, sterols, terpenoids, phenols, quinones, coumarins and cardiac glycosides. 0.53% of naringenin was confirmed by HPLC analysis method (**Anuja et al., 2014a; Janarthan et al., 2016; Rajesh et al., 2017; Pargavi and Siva Kumar 2014**). Petroleum ether extract of DQR reported optimistic phytoconstituents such as sterols, terpenoids, cardiac glycosides, tannins, proteins and amino acids, carbohydrates, phenols, coumarins, saponins and fixed oils and fats (**Janarthan et al., 2016; Rajesh et al., 2017; Kowar et al., 2010; Pargavi and Siva Kumar 2014; Prasana and Chitra 2015**). Phytochemicals including sterols, terpenoids, alkaloids, glycosides and tannins were detected in chloroform extract of DQR (**Janarthan et al., 2016; Kowar et al., 2010**). Aqueous extract of DQR revealed positive test against phytochemicals such as carbohydrates, saponins, tannins, flavonoids, proteins and amino acids, cardiac glycosides, quinones, phenol, alkaloids and gums and mucilages respectively in the extract (**Janarthan et al., 2016; Rajesh et al., 2017; Kowar et al., 2010**). Phytoconstituents named as alkaloids, glycosides, phytosterols, tannins, carbohydrates, saponins, proteins and amino acids, phenol, flavonoids, coumarins, terpenoids, cholinergic acid and fixed oils and fats were detected in the methanolic extract of DQR. Chemical compounds such as alkanes, alkenes, amines, carboxylic acid, denaturated amines, alkenes, alkanes and alkynes were recorded at peak value of 1447, 815, 3436, 1722, 2360, 1626, 2917 and 2125 by FT-IR spectrum. Ultra violet- visible displayed peak at 279 and 214 nm with absorption of 2.60 and 0.92 respectively for methanolic extract. The phytochemicals, alkaloids, carbohydrates, saponins, phenols and flavonoids were detected in the methanolic extract of DQ leaves (DQL) (**Kowar et al., 2010; Pargavi and Siva Kumar 2014; Prasana and Anuradha, 2016; Runa et al., 2013; Prasana and Chitra, 2015**). The physicochemical investigation of Total ash value, water soluble ash value, and acid insoluble ash value, extractive value of water and alcohol extractive value of DQR and fronds ranged as 8.37-9.93%, 4.13-6.93%, 3.48-4.49%, 7.78-13.94% and 4.13-9.87%. The sulphated ash and moisture content found to be 5 and 3% respectively. As the plant rich in phytochemicals, DQ may responsible in treating various health affecting diseases (**Selvi et al., 2016; Kowar et al., 2010; Vikas et al., 2016**).

Table 4: Phytochemistry of DQ

Name of the phytochemical	Part of the plant	Type of extract	Reference
<ol style="list-style-type: none"> 1. Friedelin 2. Epifriedelinol 3. β-amyrin 4. β-sitosterol 5. β-sitosterol 3-β-D-glucopyranoside 6. Naringin 7. Naringenin 	DQR	Methanol	Ramesh et al., 2001; Prasana et al., 2019
<ol style="list-style-type: none"> 1. 3,4-dihydroxybenzoic acid 2. Acetyl lupeol 	DQR	Ethanol	Khan et al., 2007a
<ol style="list-style-type: none"> 1. 2,4,6-cycloheptatrien-1-one,3,5-bistrimethylsilyl 2. 1,2-bis(trimethylsilyl) benzene 3. 2-propanol, 1-chloro-3-(1-methylethoxy)- 4. Silane,1,4-phenylene bis(trimethyl) 5. 2,6-lutidine 3,5-dicholoro-4-dodecylthio- 6. 1-heptyn-4-ol 7. 2-propanol,1-chloro-3-propoxy- 8. 6-amino-5-cyano-4-(3-iodophenyl)-2methyl-4H-pyron-3-carboxylic acid ethyl ester 9. 2-myristynol-glycinamide 10. Benzene,2-(tert-butyl dimethyl silyl)-1isopropyl)-4-methy 11. 1,2,4-benzene tri carboxylic acid, 1,2dimethyl ester 	DQR	Ethanol	Nithin et al., 2020
<ol style="list-style-type: none"> 1. Tetrahydroisovelleral 2. 7, 10, pentadecadiynoic acid 	Whole plant	Methanol	Rajesh et al., 2016

3. Phosphoric Acid, octyl diphenyl ester			
4. Octicizer			
5. Phosphoric acid, 2-ethylhexyl diphenyl ester			
6. Quercetin 7, 3', 4' Trimethoxy			
7. 1, 30-Triacotanediol			
8. Ergost-5-en-3-ol, (3a'-			
9. Lucenin 2			

3. Pharmacological activities of DQ

3.1. Antimicrobial activity

Rajesh et al., reported the antibacterial properties of DQ against scale rots in pythons by collecting wound swabs from Reticulated Python (*Python reticulatus*) and Indian Rock Python (*Python molurus*) and cultured in appropriate media. By using the standard biochemical procedure, the isolated bacterium was identified as *E. coli* (G-ve) and *Staphylococcus aureus* (G+ve). The Kirby-Bauer/disc-diffusion method was used to screen antibiotic susceptibility against isolated bacterial strains using nine antibiotics. The test confirms that the strains were resistant to all six antibiotics and sensitive to the antibiotics enrofloxacin, ciprofloxacin, and gentamicin used in the study. The antibacterial activity was determined using the agar-well diffusion method and solvent extracts such as petroleum ether, ethanol, and aqueous. Petroleum ether extract inhibited *E. coli* and *S. aureus* the least, while ethanolic extract inhibited them the most (24.667 and 28.667). The control linezolid 30g/ml and imipenem 10g/ml were found to have a similar zone of inhibition against the isolated bacterial strains (**Rajesh et al., 2017**). K.K Seena et al., reported the antifungal and antibacterial properties of aqueous and acetone extracts of DQL and DQR. The disc diffusion method was used to demonstrate antibacterial activity against *Vibrio cholera*, and the amended potato dextrose agar medium was used to demonstrate antifungal activity against *Aspergillus* sp. The acetone extract of the DQR demonstrated greater antibacterial activity than the DQL extract, inducing a 3 cm diameter zone of inhibition. The antifungal activity of DQR acetone extract showed significant activity than that of DQL acetone extract. In both cases, the DQL acetone extract was less active than the DQR extract. In both cases, aqueous extract lacked antibacterial and antifungal activity (**Seena and Valsamma, 2018**). Another study found that isolated acetyl lupeol and 3, 4-dihydroxybenzoic acid from DQR had

antibacterial activity against six gram-ve and four G+ve bacteria using the disc diffusion method and the serial dilution technique. When compared to kanamycin as a positive control, the compound 3,4-dihydroxybenzoic acid demonstrated potent antibacterial activity against the tested bacterial strains. The presence of antibacterial activity was indicated by the MIC value of 3,4-dihydroxybenzoic acid, which was found to be 8-64 g/ml. Antibacterial activity of isolated acetyl lupeol against the tested bacterial strains was insignificant (**Khan A et al., 2007a**). Rajan Padhy et al., used agar well diffusion and disc diffusion to test the antibacterial activity of a methanolic extract of DQR against both G-ve and G+ve bacterial strains in vitro and in vivo. G+ve bacterial strains such as staphylococcus aureus MTCC 96, *S. epidermidis* (CI), *B. subtilis* MTTC 121, and *S. pyrogens* were sensitive to DQR in both methods, whereas *S. pneumonia* was resistant. *S. flexineri* MTCC 1457 was discovered to be resistant to the extract. In G-ve bacterial strains, all of the tested strains were found to be sensitive to methanolic extract of DQR. The test compound's MIC value ranged from 0.62 mg/ml to 1.25 mg/ml. In vitro methanolic extract inhibited more than in vivo methanolic DQR extract. The study looked for phytochemicals like flavonoids, phenols, saponins, tannins, sterols, and carbohydrates. Saponins were found to be responsible for a wide range of antibacterial activity (**Padhy and Dash, 2015**). Using the agar well diffusion method, an Ethylacetate extract of the tuber and DQL of DQ was tested for antimicrobial activity against *Candia albicans* and multidrug bacterial strains *S. aureus*, *E. coli* pGLO, *E. coli* pUC19, *Staphylococcus saprophyticus*, and *E. coli* DH-5. The tuber extract at 100g/ml demonstrated microbial activity against all strains, but not against *Staphylococcus aureus*. The DQL extract 100 mg/ml demonstrated microbial activity of strains, but it failed to demonstrate a positive test against *E. coli* (pUC19) and *staphylococcus aureus*. The tuber extract at 10 mg/ml did not show any activity, but the DQL extract showed positive results against strains such as *Candia Albicans*, *E. coli* (DH-5), and *Staphylococcus saprophyticus*. The inhibition zone of diameter (451) mm is observed for 100 mg/ml DQL extracts against *Staphylococcus saprophyticus* and *E. coli* (DH-5). The results showed that the DQL extract was highly active against the microorganisms tested. When compared to DQL extract, tuber extract at 100 mg/ml demonstrated broad-spectrum activity (**Anamika et al., 2015**). The disc diffusion method was used to test the antimicrobial activity of the DQR, fertile and infertile leaves of DQ against clinically isolated 24 *Neisseria gonorrhoeae* and six *Neisseria gonorrhoeae* strains of WHO [WHO-C, G, L, O, B, F] and the results were compared with penicillin and ciprofloxacin. Penicillin resistance was found in 14 clinical isolates [1-11, 15-20, and 23] as well as WHO strains of WHO-O and WHO-L. Ciprofloxacin was resistant to all isolates as

well as WHO-L. DQ parts tested negative for resistance to clinical isolates and WHO strains. When compared to penicillin, the parts such as fertile and infertile leaves and DQR were susceptible to 7, 8 and 10 clinical isolates among the 24 and WHO strains of WHO-O and WHO-L, respectively. Clinical isolates such as 1-3, 5-11, 18, 23 and 1-3, 5-11, 18, 22 and 23 were found to be susceptible to infertile and fertile leaves. When compared to ciprofloxacin, the DQR showed high sensitivity to clinical isolates 1-11, 18 and 23 and all parts showed high sensitivity to WHO-L strain (**Shokeen et al., 2005**). Using the disc diffusion method, extracts such as acetone, benzene, chloroform, water, ethanol and petroleum ether were tested for antibacterial activity against isolated urinary tract infecting (UTI) bacteria. Acetone had the highest antibacterial activity against gramme +ve bacteria, *Streptococcus pyogenes* and *Enterococcus faecalis*, with maximum zones of inhibition of 22 mm and 8 mm, respectively. The inhibition zone of ethanol extract against *Pseudomonas aeruginosa*, a G-ve bacteria, was reported to be seven millimetres. The antibiotic amikacin had a zone of inhibition of 23 mm against *Streptococcus pyogenes* (**Mithraja et al., 2012**). The inhibition zone of ethanol extract against *Pseudomonas aeruginosa*, a G-ve bacterium, was reported to be seven millimetres. The antibiotic amikacin had a zone of inhibition of 23 mm against *Streptococcus pyogenes* (**Prasana et al., 2014**). Using the disc diffusion method, the researchers tested the antibacterial activity of petroleum ether extract, chloroform extract and Ethylacetate extract of DQR against four G+ve and six G-ve bacteria. The extracts at 150 mg/disc demonstrated less antibacterial activity than the standard kanamycin at 50 mg/disc. The chloroform and Ethylacetate extracts were more active than the petroleum ether extract. The extracts' MIC ranged from 16 to 64 µg/ml, respectively (**Khan et al., 2012**).

3.2. Cytotoxicity

The cytotoxic activity of petroleum ether, chloroform, Ethylacetate, and ampicillin trihydrate extracts against brine shrimp nauplii was investigated using the brine shrimp lethality bioassay method. According to the study, as the concentration of the sample increases, the death of the nauplii increases respectively. The extracts' and standard's LC₅₀ values were 22, 16.5, 16.5 and 11.7µg/ml, respectively. The cytotoxicity of chloroform and Ethylacetate extracts was found to be greater than that of petroleum ether extract. All of the extracts had lower toxicity and higher LC₅₀ values than the standard ampicillin trihydrate (**Khan et al., 2012**). Another study used brine shrimp lethality bioassay to assess the cytotoxic activity of carbon tetrachloride soluble fraction, Ethylacetate, petroleum ether and aqueous fractions of DQR against brine shrimp nauplii. Carbon tetrachloride was the most cytotoxic of the

fractions, with an LC₅₀ value of 30.31 µg/ml. The LC₅₀ values for aqueous fractions, Ethylacetate and petroleum ether were 41,041.30 µg/ml, 569.39 µg/ml and 2,380 µg/ml respectively. Vincristine sulfate's LC₅₀ value has been reported to be 0.544 µg/ml (**Mohanta et al., 2013a**).

3.3. Antioxidant

The antioxidant activity of was evaluated solvent extracts DQR of chloroform, petroleum ether, methanol and aqueous using DPPH radical scavenging activity and ferric reducing antioxidant power (FRAP) assay model. Among the extracts, the methanolic extract showed potent antioxidant activity (94.37%) at a concentration of 500 ppm (>90%) when correlated with the standard α -tocopherol (500 ppm (86.27) (**Beknal et al., 2010**). DQR methanolic extract was tested for antioxidant activity using DPPH radical scavenging activity, hydrogen peroxide (H₂O₂), nitric oxide (NO), hydroxyl ion radical (OH), and ABTS scavenging assays. By assay methods, DQR extract demonstrated significant scavenging activity than standard butyl hydroxyl toluene (BHT) (**Jinu et al., 2014**). The antioxidant activity of a methanolic extract of DQR and fronds was determined using a DPPH radical scavenging assay. Scavenging activity of DQR and fronds was found to be 26.19 2.20 and 21.94 1.49 percent, respectively. Using TLC, the phytochemical screening revealed alkaloids, saponins, terpenoids, phenolics, anthraquinones, and tannins. The total phenolic content (TPC) of methanol extracts of DQR and frond was found to be between 37 and 100 µg GAE/g and the total flavonoid content (TFC) of methanolic extract of DQR was reported to be 36.74 2.17 µg QE/g, with no flavonoids detected in methanolic frond extract (**Amoroso, 2017**). The aqueous tuber extract of DQ demonstrated potent DPPH, Nitric oxide, ABTS and hydroxyl radical scavenging activity with IC₅₀ values of 105.78, 57.07, 27.32 and 26.54 µg/ml, respectively. At a concentration of 120 µg/ml, the Fe³⁺ reducing power assay and the phosphomolybdenum reduction assay revealed an increase in radical reduction of 0.58±0.40 and 0.44±0.80, respectively when compared to the standard ascorbic acid. As the concentration of the extract increases, so does its antioxidant property. The total phenolic and flavonoid content of GAE was found to be 4.2951.23 µg/ml and QE was found to be 24.5640.86 µg/ml (**Sivaraj et al., 2018**). DQ aqueous extract (AEDQ) and methanolic extract (MEDQ) demonstrated antioxidant activity via DPPH radical scavenging activity, superoxide radicals, and reducing power activity. The IC₅₀ value of MEDQ's in vitro antioxidant activity was given as 53.6, 42.9 and 49.8 µg respectively and the IC₅₀ value of AEDQ was given as 66.2, 67.2 and 41.05 µg. Standard ascorbic acid had IC₅₀ values of 12.39 µg, 7.6 µg and 4.3 µg

respectively. The methanolic extract of DQ had a higher total phenolic content of 95.972 $\mu\text{g}/\text{GAE}$ and a higher total flavonoid content of 81.03 $\mu\text{g}/\text{QE}$ (Das et al., 2014a). The various fractions such as Ethylacetate, aqueous, petroleum ether, and carbon tetrachloride soluble fraction were tested antioxidant activity using DPPH free radical scavenging method. IC₅₀ value of the fractions was found to be 38.25 $\mu\text{g}/\text{ml}$, 124.39 $\mu\text{g}/\text{ml}$, 161.68 $\mu\text{g}/\text{ml}$ and 62.9868 $\mu\text{g}/\text{ml}$ respectively. The highest scavenging activity was resulted by the Ethylacetate soluble fraction and carbon tetrachloride fraction. The IC₅₀ value of standard butyl hydroxyl toluene (BHT) was found to be 35.52 $\mu\text{g}/\text{ml}$. The Ethylacetate soluble fraction's antioxidant activity was close to the standard butyl hydroxyl toluene (BHT) (Mohanta et al., 2013a). Chaity et al. revealed the aqueous fraction and crude methanol extract of DQR and fertile foliage fronds of DQ showed significant scavenging property against DPPH, ABTS, FRAP assay and hydrogen peroxide assay respectively. The aqueous fraction resulted potent scavenging activity than the crude methanolic extract of both the plant parts (Chaity et al., 2016). In vitro antioxidant activity of methanolic extract of DQR was performed using different in vitro models such as total antioxidant capacity, reducing power assay, nitric oxide scavenging and hydrogen peroxide radical scavenging activity. The activity was tested using 100, 200 and 300 $\mu\text{g}/\text{ml}$ of doses respectively as compared with the standard ascorbic acid. The extract at 300 $\mu\text{g}/\text{ml}$ showed potent activity against in vitro models found to be 54.88 ± 0.17 , 58.07 ± 1.97 , 62.77 ± 0.58 and $44.09 \pm 1.03\%$ and the standard ascorbic acid at 300 $\mu\text{g}/\text{ml}$ reported to be 54.53 ± 0.57 , 62.80 ± 2.02 , 54.60 ± 0.45 and 57.87 ± 0.71 respective to the models used in the study. Among the in vitro models, nitric oxide showed the highest antioxidant activity. The IC₅₀ values of methanolic extract of in vitro model were found to be 230, 230, 180 and 240 $\mu\text{g}/\text{ml}$ respectively (Prasana and Chitra, 2014b).

3.4. Anti-inflammatory activity

Janaranjani B *et al.*, screened the anti-inflammatory activity of ethanolic extract of DQR against carrageenan-induced paw oedema rats using various concentrations (100, 200 & 500 mg/kg) of extract. The extract at 500 mg/kg showed a higher (58%) percentage of paw oedema inhibition than the standard drug dexamethasone (40%). The inhibition of paw oedema by extract at 100 and 200 mg/kg was 21% and 33% respectively (Janarajani et al., 2014). Fertile fronds (FF) of DQ were evaluated for their Anti-oedematous activity by using ethanolic extract against histamine-induced paw oedema rats, carrageenan-induced, and also by cotton pellet granuloma formation in rats. The extract at 500 mg/kg dose showed a greater reduction of carrageenan-induced and histamine-induced paw oedema in rats (71.76% &

66.67%). Test results were compared with the standard indomethacin 10 mg/kg (88.24% & 68.89%) respectively in both cases. FF on oral administration reduces both dry weight and wet weight of granuloma tissue. The dose at 500 mg/kg showed inhibition of both the exudative phase (53.2%) and the proliferative phase (60.18%) of inflammation (**Anuja et al., 2014b**). *In vitro* and *in vivo* anti-inflammatory property of water and methanol extract of DQR was reported against the albumin denaturation, carrageenan-induced paw oedema and membrane-stabilizing methods. The extracts inhibited paw oedema in a dose-dependent manner (100 & 150 mg/kg) and inhibited the COX-1 and COX-2, protein denaturation and hemolysis at 100 mg/ml. The methanolic extract showed potent activity than the water extract (**Das et al., 2014a**). Methanolic extract of DQR exhibited *in vitro* anti-inflammatory activity in a dose-dependent manner for both test extract and the standard diclofenac (100, 200 & 300 mcg) against human red blood cell (HRBC) membrane stabilization method. The percentage of membrane stabilization of test extract and diclofenac was reported 33.64%, 34.14%, 34.94% & 35.52%, 39.09%, 41.62% respectively 100, 200 & 300 mcg. Maximum activity was reported at 300 mcg in both the plant extract and standard diclofenac (**Prasana and Chitra, 2015c**).

3.5. Analgesic activity

Ethanol extract of fertile fronds (FF) of DQ showed potent analgesic activity in a dose-dependent manner of 100, 200 and 30 mg/kg respectively. Notably, FF reduced acute and delayed phases of capsaicin-induced nociception, acetic acid-induced writhing, formalin-induced pain and hot plate test in mice. The activity was compared with standard drugs aspirin (100mg/kg) sodium salicylate (100 mg/kg) and morphine (7.5 mg/kg) respectively (**Anuja et al., 2014b**). Milon C Mohanta et al., studied the anti-nociceptive activity of crude methanolic extract and various solvent-soluble fractions of DQR by radiant heat tail-flick and acetic acid-induced writhing inhibition methods in swiss albino mice. Aqueous soluble fraction and carbon tetrachloride fraction (400 mg/kg) of crude methanol extract, revealed the potent anti-nociceptive activity of 40.99%, 45.64% and 34.9% of acetic acid-induced writhing inhibition in peripheral anti-nociceptive method when compared with that of standard diclofenac 51.68% of writhing inhibition. In the radiant heat tail-flick method of central anti-nociceptive, the crude methanolic extract (400 mg/kg), petroleum ether fraction (400 mg/kg) and carbon tetrachloride fraction (400 mg/kg) reported better analgesic activity of 63.92%, 64.92% and 51.4% increase in the reaction time respectively at 1 hour after administration of sample and increase in reaction time was observed with standard morphine

(75%). At 90-minute methanolic crude extract and petroleum ether fraction (400 mg/kg) showed extension of tail-flick time by 34.49% and 36.10% and standard morphine reported as 37.94%, respectively (**Mohanta et al., 2013b**). The study evaluated the anti-nociceptive property of hexane extract (HDQ), crude ethanol extract and Ethylacetate extract (EDQ) of the DQR against swiss albino mice and wistar albino rats using glutamate-induced nociception, tail immersion, capsaicin-induced nociception and tail-flick methods. The extracts DQ (100, 200 & 300 mg/kg), HDQ (50, 100 & 200 mg/kg) and EDQ (25, 50 & 100 mg/kg) showed dose-dependent inhibition of nociception against methods compared with standard morphine (7.5 mg/kg) respectively (**Anuja et al., 2014a**).

3.6. Pesticidal and pest repellency

Pesticidal & pest repellency activity of DQR was tested for protecting the stored seeds & flour-based items in tropical and subtropical regions against *Tribolium castaneum*. The study reported that the chloroform soluble fraction of ethanol displayed notable pesticide and pest repellency activity. Ethylacetate, petroleum ether, methanol soluble fractions did not show the pesticide and pest repellency activity against the *Tribolium castaneum*. The isolated 3, 4-dihydroxy benzoic acid from Ethylacetate fraction showed negative activity against the tested organism (**Khan et al., 2014**).

3.7. Antidiarrhoeal activity

Rajan padhy et al., study confirmed the anti-diarrhoeal activity of methanol extract of DQR (MEDQ) castor oil inducing diarrhea along with gastrointestinal motility and enteropooling in albino rats. The DQR methanol extract showed dose-dependent reduction action against castor oil-induced diarrhea at 100 mg/kg and 200 mg/kg (61.89 & 66.25%). The standard drug Loperamide (5 mg/kg) inhibited in the range of 83.1% respectively. The extract reduced the charcoal distance travelled in dose manner 100 mg/kg (36.08%) and 200 mg/kg (54.88%) and the standard drug Loperamide (5 mg/kg) showed a 72.74% decrease of charcoal meal travel through the gastrointestinal tract by using gastrointestinal motility test. The percentage decrease of enteropooling by MEDQ of both the doses (100 & 200 mg/kg) as 57.69 and 66.92% w/w and Loperamide (5 mg/kg) inhibited 74.61% when induced by castor oil. The study concluded that flavonoids and glycosides, saponins, reducing sugars, tannins, and tannic acids in the extract were responsible for the activity (**Padhy et al., 2016**).

3.8. Anthelmintic activity

Gauri kaustubh Kulkarni et al., reported the anthelmintic property of DQL and DQR by using mature earthworms and piperazine citrate as a standard. Alcoholic extract of DQL and DQR showed an increase in the period of paralysis and death of the worm at doses 2.5, 5, 10, 25 and 50 mg/ml compared with the standard piperazine citrate (10 mg/ml). The test extracts showed high significant anthelmintic activity than the standard (**Kulkarini et al., 2010**). Various doses (10, 20, 30, 40 & 50 µg/ml) of methanolic extract of DQL demonstrated the anthelmintic activity using adult earthworms (*Pherentima Posthuma*). The activity was determined by parameters such as time of paralysis and time of death worms. The test extracts compared with the standard drug albendazole (15µg/ml). The activity was increased as the concentration of the extract increased. The paralysis and death time of the earthworms by extract reported as 6-23.87 and 53.67-127.67 minutes respectively. The time paralysis and death time of earthworms by standard albendazole reported 35.33 minutes and 71.33 minutes respectively for the worm's death. The extract showed potent anthelmintic activity than the standard drug (**Ali et al., 2013**).

3.9. Antidiabetic and hypolipidemic activity

G. Prasana et al., evaluated *in vitro* antidiabetic study of methanol extract of DQR. The activity was determined by assay methods such as alpha-amylase and glucose uptake assay. L6 rat myogenic cells were subjected to the glucose uptake assay. The inhibition of alpha-amylase was significantly increased as the extract's concentration increases (25, 50 & 100 µg/ml). The percentage inhibition reported by the concentrations 40.1±2.6, 65.7±4.11 and 79.8±3.5 in a concentration-dependent manner. Standard metformin (0.1µg/ml) reported 85.07±7.6% of inhibition. The standard metformin (0.1µg/ml) in glucose uptake assay increased the glucose uptake level of 7.07±0.30 and 4.81±0.31 in the presence or absence of insulin. Plant extract in the presence of insulin elevated the glucose uptake to 6.13±0.28, 6.23±0.19, 6.39±0.54 and 6.73±0.41, and in the absence of insulin, it resulted as 5.02±0.32, 4.98±0.27, 4.06±0.16 and 3.14±0.21 at concentrations of 5.0, 10, 20 and 40 µg/ml respectively. The standard drug showed potent activity than the extract. The plant DQR extract showed significant antidiabetic activity by preventing hyperglycemia and controlling lipid metabolism (**Prasana et al., 2019**). Oral administration of ethanol extract and chloroform extract of DQR at 400 mg/kg and glibenclamide 5mg/kg lowered the blood sugar level and increased rats' body mass compared to diabetic control rats. Respectively the test extracts and standard drug reversed the lipid profile levels than the control group.

Additionally, the study is also confirmed by the histopathological examination of the pancreas (**Rajimol et al., 2014**).

3.10. Antifibrotic activity

Karishma desai et al., reported the antifibrotic activity of DQ methanolic extract on oral submucous fibrosis. The study revealed that the methanolic extract of DQ significantly reduces the cell viability of the Human buccal mucosa fibrosis (HBSF) in a dose-dependent manner (100-400 µg/ml) when compared with chymotrypsin, the drug used for submucous fibrosis (**Desai et al., 2019**). Another study reported the anti-fibrotic property of crude extract and fractions of Ethylacetate (EDQ), hexane (HDQ) and butanol (BDQ) using different doses (25, 50 & 100 µg/ml) against the isolated rat hepatocytes and RAW 264.7 cells. Ethylacetate fraction at 100 µg/ml showed potent *in vitro* activity than HDQ and BDQ compared with standard drugs silymarin and diclofenac sodium (100 µg/ml). *In vivo* oral administration of EDQ (100 µg/ml) gradually increased catalase (CAT), superoxide dismutase (SOD), Nrf2 levels of CCl₄ induced rats. Decreased amount of malondialdehyde (MDA), iNOS, COX-2, and TNF- α , was observed when compared to CCl₄ treated animals. Histology and immune histochemistry results reported that the animals treated with EDQ (100 µg/ml) and silymarin (100 µg/ml) revealed minor fibrotic changes, lack of pseudolobulization and reduction in TIMP-1, α -SMA and collagen deposition and elevated the levels of Nrf2 r (**Anuja et al., 2018**).

3.11. Antipyretic activity

The Ethylacetate and petroleum ether fractions of ethanol extract of DQR at 80 mg/kg showed potent antipyretic activity when compared with the standard aspirin (10 mg/kg) after 3 hours of elevated body temperature (0.5 ml/kg b.w of boiled milk administered through intraperitoneal (I.P). Both the fractions reported significant activity by lowering the body temperature (**Khan et al., 2007b**). The antipyretic activity of methanol extract of DQR at doses 100, 250 and 500 mg/kg were tested against rats induced subcutaneously with brewer yeast suspension at a dose of 10 ml/kg (which increases the rectal temperature). The extract at 500 mg/kg revealed a significant reduction of rectal temperature than 100, 250 mg/kg and standard paracetamol 200 mg/kg at a time interval of 3 hours respectively (**Janaranjani et al., 2014**).

3.12. Thrombolytic activity

The aqueous soluble fraction (AQSF) and petroleum ether soluble fraction (PESF) of methanolic DQL showed significant thrombolytic activity (34.38 and 34.27%) when compared with the standard streptokinase (41.05%) and negative control distilled water (3.31%) of clot lysis (**Ramjan et al., 2014**).

3.13. Membrane stabilizing

Chaity et al., performed membrane stabilizing activity of crude methanolic extract and fractions of DQR and DQL respectively. The crude methanol extract of the DQR showed potent membrane stabilizing activity than the DQL. The moderate membrane stabilizing was showed by petroleum ether fraction of both the parts used in the study (**Chaity et al., 2016**).

3.14. Anti dermatophytic activity

The study evaluated the antidermatophytic activity of various solvent extracts of DQR against different pathogenic fungi using disc diffusion and agar dilution methods. Among the extracts, di-ethyl ether with semi-polarity gave a transparent zone of inhibition towards the pathogenic fungi. The highest zone of inhibition was seen against *Trichophyton mentagrophytes* (25 mm diameter). The presence of triterpenes and coumarins DQR may responsible for the antidermatophytic activity of DQR solvent (**Nejad and Deokule, 2009**).

3.15. Mosquito repellent activity

The extracts, such as petroleum ether (PET), methanol (MET), dichloromethane (DCM) and aqueous extract (AQ), studied for mosquito repellent activity against the adult mosquito species *Culex quinquefasciatus* and *Aedes aegypti*. The activity increases as the concentration of the extracts increases. Aqueous extract at 500 ppm of concentration showed a massive reduction of the larva population than PET, MET and DCM. PET at a concentration of 160 mg resulted in the 'Knock down' effect within 20 minutes (**Marathe et al., 2011**).

3.16. Cataractostatic activity

Cataractostatic activity of ethylacetate and methanol extracts of DQ tuber evaluated against formation of lens cataracts in isolated goat lens by using photographic evaluation and quantitative catarostatic analysis. The ethylacetate extract showed better activity in inhibition of cataract formation than that of methanolic extract of DQ tuber. Ethylacetate extract inhibited the cataract formation in a dose-dependent manner. The study claimed that ethylacetate extract at 80 µg/ml has shown 100% inhibitory activity in cataract formation and also may prevent diabetic cataract (**Chowdhury et al., 2017**).

3.17. Hepatoprotective

The methanolic extract of DQR showed significant hepatoprotective activity by increasing the percentage of cell viability and decreasing the levels of MDA, SGOT & SGPT, and also by increasing the levels of GSH and protein in hepatocytes in a dose dependent manner (100, 250, 500 mg/ml) (**Devika and Prasana, 2016**). The hepatoprotective activity of DQ fronds of hydroalcoholic extract and its fractions and isolated compound (Dq-4) from ethylacetate (EA) fraction were evaluated by *in vivo* and *in vitro* methods. *In vivo* results reported that the hydrochloric extract (400 & 200 mg/kg) and ethylacetate (EA) fraction (74.55 mg/kg) exhibited significant hepatoprotective activity by gradually reducing the level of total bilirubin, hepatic enzymes (ALP, ALT & AST) and improved albumin and serum total protein levels and also increasing and decreasing the levels of GSH and TBARS against toxic CCl₄ (1 ml/kg) induced animals. *In vitro* hepatoprotection of HepG2 cells against CCl₄ (1%) induced toxicity was performed using the MTT reduction test and trypan blue technique. Isolated compound Dq-4 at a dose level of 50 µg/ml showed the highest protection of cell viability against CCl₄ (1%) induced cells. The hydrochloric extract and EA fraction at a dose level of 100 µg/ml reported the cell protection (**Kamboj and Kalia, 2013**).

3.18. Urolithiasis

Urolithiasis activity was investigated by using different solvent extracts of DQR against 0.2% ethylene glycol aqueous induced male wister rats. The activity was performed by treating with extracts of DQR and spironolactone and cystone for 10 days at a dose of 25 mg/kg body weight. The alcohol and water extracts of DQR and cystone & spironolactone increased the volume of urine output and reduced the kidney weight than the diseased control group and also decreased the level of GAO and LDH enzymes which responsible for conversion of glycolate to oxalate which results in urolithiasis. Further, histopathology studies reported that alcohol and water extracts of DQR and cystone and spironolactone gradually decreased the accumulation of calcium oxalate crystals respectively. Chloroform and petroleum ether extract showed negative results towards the activity tested. By all these estimations, it is concluded that alcoholic and water extract of DQR showed significant activity and helpful in treating renal calculus (**Soodam and Beknal, 2012**).

3.19. Neuropharmacological activity

Alam khan et al., investigated the neuropharmacological activity of the DQR against the light-dark test effect of nikethamide-induced toxicity, diazepam-induced sleep and forced swimming test. Ethanol extract of ethylacetate and petroleum ether soluble fraction at doses

of 50,100 and 200 mg/kg body weight were administered intraperitoneally for albino mice. Both the fractions have increased the duration of diazepam-induced sleep. The fractions were slowed down the time to cause death in mice compared to nikethamide (at high dose causes animal death) (Khan et al., 2009).

3.20. Antiarthritic activity

S. Saravanan et al., demonstrated antiarthritic activity of DQR water extract against adjuvant-induced arthritic female wistar rats. The study concluded that the standard indomethacin (2 mg/kg) and test extract (200 & 100 mg/kg) gradually lowered paw thickness and elevated body weight compared to the arthritic animals. The parameters such as plasma protein-bound carbohydrates, liver lysosomal enzymes, ROS, urinary degradative collagen levels, plasma and lysosomal enzymes in neutrophils and pro-inflammatory cytokines [TNF- α AND IL-1 β] predominantly lowered by standard indomethacin and also by DQR water extract in a dose dependent manner compared with control and adjuvant-induced arthritic animals. The test extract improved the degree of anti-inflammatory cytokine IL-10 when compared to arthritic animals (Saravanan et al., 2013).

3.21. Toxicity study

Rajan et al., reported the acute and sub-acute toxicity studies of methanolic extract of DQR using wistar albino rats and swiss albino mice respectively. The edge dose of 2000 mg/kg of methanolic extract was induced to swiss albino mice and kept under observation for 7 days. In the acute toxicity model, a daily dose of 1g/kg body weight of methanolic extract was administered to wistar albino rats for 28 days respectively. The study reported that DQ methanolic extract as a safe drug for use and 2000 mg/kg body weight dose resulted ALD₅₀ under the Globally Harmonized classification system (GHS) category 5 safe dose, as per OECD guideline 423 (Annexure 2d) as there was no mortality in samples during Acute toxicity studies. There were no significant marked changes observed in haematological parameters during sub-acute toxicity tests (Padhy et al., 2017).

3.22. Antifertility

Banani das et al., reported the anti-fertility activity of DQR solvent extracts of like petroleum ether, ethylacetate, acetone and methanol against female wistar albino rats. Among the tested extracts the methanolic extracts at dose of 200 mg/kg showed significant anti-implantation and abortifacient activity by changes in implantation sites' mechanism changed hormone

levels, and rise in uterine muscle contraction when compared with the control animals (**Das et al., 2014b**).

4. Conclusion

This review reports the traditional uses, phytoconstituents and pharmacological properties of DQ. The presence of numerous bioactive compounds in the plant provided the greater eye-opening activity against various life-threatening ailments. The plant demonstrated potent *in vitro* and *in vivo* activity against diseases such as analgesic, anti-fertility, antimicrobial, anthelmintic, antipyretic, anti-inflammatory, antidiabetic, hypolipidemic, thrombolytic, antioxidants, antiarthritic, urolithiatic, cytotoxic, mosquito repellent, antiulcer, antidermatophytic, anti-arthritis, pest, and pest repellency among others. In the future, more experimental animal studies and clinical trials on isolated plant compounds should be conducted in the development of new drugs in medicine.

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