Trop J Nat Prod Res, August 2024; 8(8): 7930 - 7940 **ISSN 2616-0684 (Print)**
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Review Article

Dexamethasone Induction of Metabolic Syndrome and Remediation By Medicinal Plants: A Systematic Review

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ARTICLE INFO

Article history:
Received 05 June 2024
Revised 07 June 2024
Accepted 20 June 2024
Published online: 01 September 2024

ABSTRACT

Dexamethasone, a synthetic glucocorticoid, is clinically used during allergic reactions and autoimmune disorders. Long-term usage, at high doses, has however been associated with detrimental effects including the development of metabolic syndrome (MS), thus, it is employed in experimental induction of MS in animal models. Medicinal plants are rich in phytochemicals, naturally occurring chemicals in plants, that have been shown to have health-promoting properties that mitigate several disease conditions. This systematic review aimed to identify the effectiveness of medicinal plants in mitigating the complications associated with MS induced by dexamethasone. The preferred reporting items for systematic review and meta-analysis protocols (PRISMA) were employed in this study. A literature search was conducted between October and November, 2023 using electronic databases to identify studies related to dexamethasone, metabolic syndrome, and medicinal plants using search words such as dexamethasone, metabolic syndrome, and medicinal plants. A total of thirty-four experimental studies were retrieved and systematically analyzed. The studies consistently demonstrated that dexamethasone administration is associated with the development of MS and that medicinal plants were efficacious in reversing the adverse effects of dexamethasone-induced MS. However, the mechanisms involved in reversing the adverse effects require further elucidation, particularly at the molecular level.

***Keywords*:** Metabolic syndrome, Dexamethasone, Medicinal plants, Remediation, Animals.

Introduction

Metabolic syndrome (MS) is a cluster of abnormalities that increase the risk of type 2 diabetes mellitus, cardiovascular diseases, and other chronic diseases. It consists of a combination of conditions ranging from central obesity, insulin resistance, hyperglycemia, hypertension, and dyslipidemia among others.[1-4] Metabolic syndrome can be caused by many factors, including genetic predisposition, environmental factors, and a sedentary lifestyle.[5] Metabolic syndrome has been revealed as a significant driver of the prevailing cardiovascular crisis globally and leads to premature death.[6] Prominent features of MS are central obesity (45.1%), elevated systolic blood pressure (42.6%), and increased High-density Lipoprotein cholesterol (40.2%). [6] In fact, dyslipidemia has a prevalence of 25.5% in Africa.[7]

The use of synthetic glucocorticoids, such as dexamethasone, plays a major role in the precipitation and worsening of metabolic syndrome.[8] Dexamethasone has very high anti-inflammatory and immunosuppressive properties, and it is widely used for the treatment of many medical issues ranging from autoimmune disorders, allergic reactions, cancer, and many others.

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Citation: Shittu ST, Ogundele OJ, Shittu SA, Isehunwa GO, Afolabi AO, Lasisi TJ. Dexamethasone Induction of Metabolic Syndrome and Remediation By Medicinal Plants: A Systematic Review. Trop J Nat Prod Res. 2024; 8(8): 7930-7940 https://doi.org/10.26538/tjnpr/v8i8.1

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Although its use is beneficial, long-term usage and high-dose administration have been linked to the development of MS and other pathological conditions[9,10] including visceral adiposity, hypertension,[11] insulin resistance, hyperglycemia, dyslipidemia,[12] immunosuppression, and osteoporosis.[13,14] The mechanism of action of dexamethasone in the development of metabolic syndrome includes alterations in glucose metabolism (via impaired insulin signaling), adipose tissue function, and cardiovascular functions. [9]

Phytochemicals, which are bioactive compounds contained in medicinal plants, have gained prominence over the years. Plants produce these naturally occurring compounds to protect themselves,[15] and these phytochemicals have been reported to be beneficial to animals and humans consuming the plants. Phytochemicals can be obtained from grains, nuts, fruits herbs, vegetables, and many more natural vegetations, and so far, thousands of phytochemicals have been identified.[15] Phytochemicals have diverse health-promoting properties, such as antioxidative, anti-inflammatory, and anti-obesity properties.[16] Phytochemicals have shown potential in modulating the key pathways involved in the development of metabolic syndrome and may provide a natural alternative for managing or preventing metabolic dysfunctions. This systematic review explored the dexamethasone induction of metabolic syndrome and the roles of medicinal plants as a means to remediate the adverse effects of dexamethasone-induced metabolic syndrome.

Materials and Methods

This systematic review adhered to the preferred reporting items for systematic review and meta-analyses (PRISMA) protocols.

Strategy for studies identification

A comprehensive search of the literature was conducted between October and November, 2023. The search was conducted using the following databases: Google Scholar, PubMed, Wiley Online, and Cochrane Library to identify relevant articles related to Dexamethasone induction of metabolic syndrome and remediation by medicinal plants. The search strategy was developed by using terms related to the metabolic syndrome and this was done through electronic databases. The search string utilized a combination of relevant keywords such as "Dexamethasone and Metabolic Syndrome", "Dexamethasone-induced metabolic syndrome and Phytochemicals", and "Metabolic Syndrome and Phytochemicals". Snowballing techniques were also used in searching for studies and it included reference list checking, and searching websites.

Study design

Inclusion and exclusion criteria

Quantitative experimental studies were considered eligible. Qualitative, non-original research, non-experimental studies, secondary reports, commentaries, editorials, and reviews were excluded.

Studies were included if they induced metabolic syndrome with dexamethasone and if the MS was treated with any form of medicinal plants. Studies that induced metabolic syndrome with chemicals other than dexamethasone, and studies that did not induce metabolic syndrome were excluded.

Outcomes

Relevant primary outcomes included studies that reported the effect of medicinal plants on dexamethasone-induced metabolic syndrome. The review elaborated on the reversal of metabolic syndrome by medicinal plants.

Selection Process

To determine the eligibility for inclusion using the population, intervention, comparison, and outcomes (PICO) template, the titles, and abstracts of the relevant and related identified research articles were examined independently. Research articles that failed to meet the eligibility criteria were eliminated. To reaffirm the article's eligibility criteria for inclusion, second and third rounds of evaluation of the selected research papers were conducted.

To describe the flow of information from database literature searches through the screening process to studies included in the review, we used a PRISMA 2020 flow diagram for visualization (Figure 1).

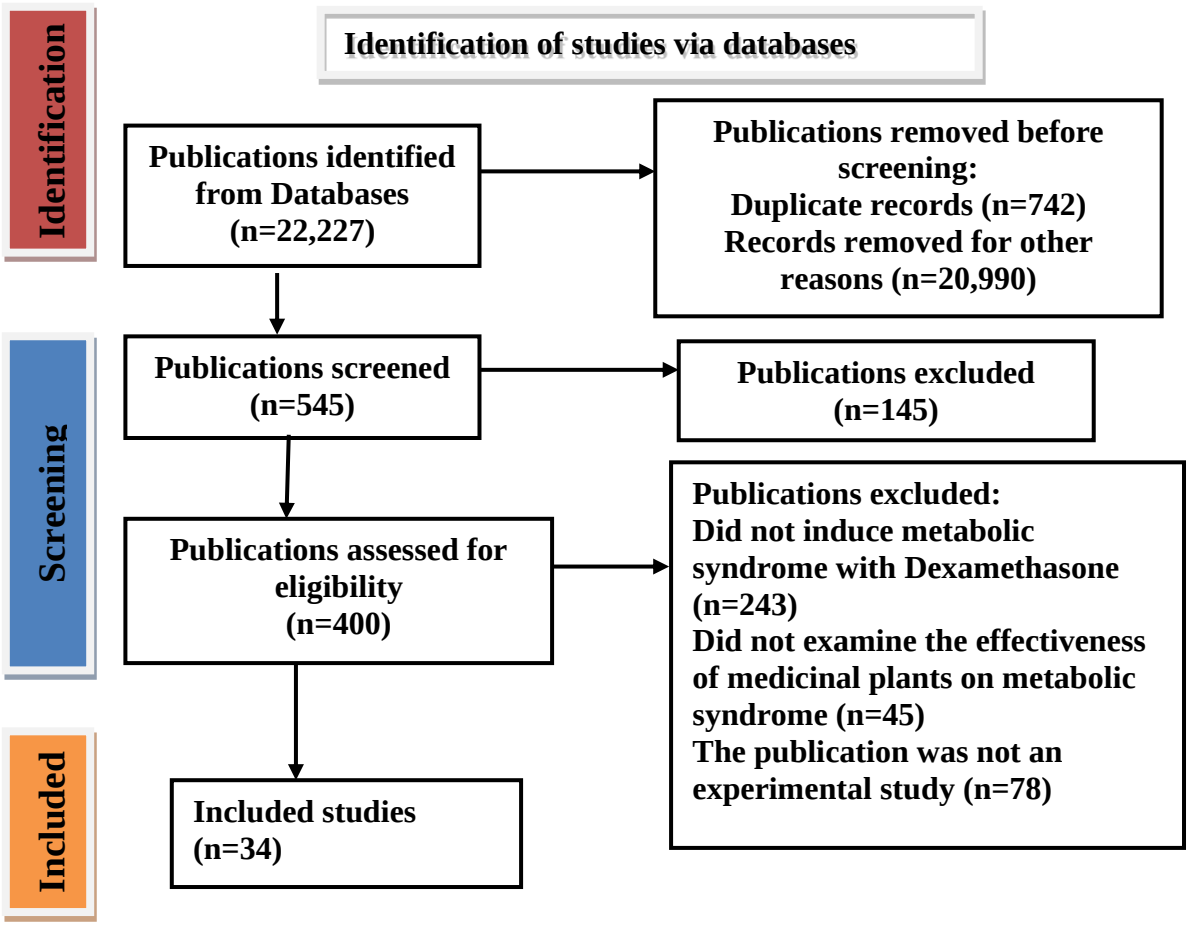

Figure 1: The PRISMA flow chart used for the study

Data extraction process

The authors and year of publication, animal characteristics, quantity and administration of dexamethasone, quantity and administration of the phytochemicals, type of metabolic syndrome induced, and effect of the medicinal plants on the animal, were all taken from each included article.

Results and Discussion

Description of the Included Studies

A total of thirty-four studies were included in this review. All the studies were published between 2010 and 2023 and were published in English language. Only animals were used in the experimental studies, however, different species of animals were used. The majority of the included studies used Wistar rats for their experiments; three of the studies used mice,[17-19] two studies used Sprague Dawley rats,[20,21]and only one study made use of Rabbits.[22]

Routes, Doses, and Duration of Dexamethasone Administration

All the included studies induced MS through the use of Dexamethasone; however, the dosage, route of administration, and duration of administration differ across all the studies. Out of all the 34 included studies, many (58.8%) induced metabolic syndrome through the subcutaneous administration of dexamethasone, some (20.58%) induced it through intraperitoneal administration of dexamethasone, few of the studies (11.76%) used intramuscular route, and only one study used intravenous route.[23]

In terms of the dosage of dexamethasone, there were also varying quantities used to induce MS. This might be due to the differences in the type of animals used, or the gender of the animals. From all the included studies, to induce MS, 11 studies used 1 mg/kg; another 11 studies used 10 mg/kg; 2 studies used 8 mg/kg; [24,25] 2 studies also used 4 mg/kg;[21,23] 3 studies used 30µg/kg;[26-28] 2 studies used 20 µg/kg;[20,29] 1 study used 1.8 mg/kg;[30] and 1 study used 3 mg/kg of dexamethasone.[31] However, 1 study[22] used as high as 150 mg/kg and this was the only study conducted on Rabbits. When the doses were categorized into 3, 50% of the study used <1 - 1 mg/kg, 41% used 2 - 4 mg/kg, and 9% used >4 mg/kg (Figure 2). With exception to the study on rabbits which gave a single high dose of dexamethasone,[22] all other studies gave multiple daily doses. These were categorized into ≤ 7 days (18%), 8-14 days (73%), and > 14 days (9%) as shown in Figure 3.

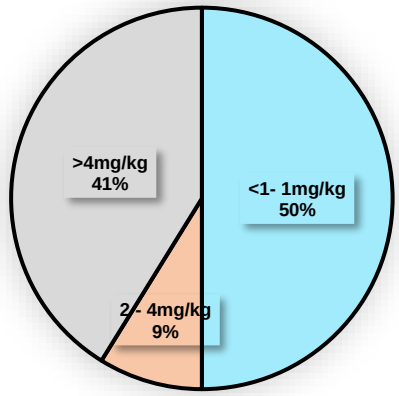

Figure 2: Doses of administered Dexamethasone

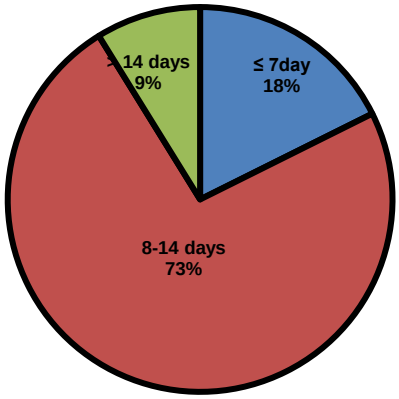

Figure 3: Number of days of Dexamethasone administration

Effect of medicinal plants on metabolic syndrome induced by dexamethasone

The outcomes of medicinal plant intervention in the dexamethasone-induced MS studies are broadly grouped into effects on body weight, liver and muscle activities, blood glucose level, lipid profile, and blood pressure. The included studies spanned 14 years, in summarizing them, they were categorized based on their year of publication as 2010-2014, 2015-2019, and 2020-2023 as shown in tables 1A, 1B, and 1C, respectively.

Effect on Body Weight

The administration of Dexamethasone in the experimental animals caused a significantly decreased body weight of the animals. Some studies found that the animals' body weight significantly decreased and was not reversed with medicinal plant administration.[17,18, 21,26,32–35] However, the administration of *Butea monosperma*,[19] *Kelussia Odoratissima*,[27] and *Cissus polyantha* [36] reversed the body weight loss caused by dexamethasone and led to a significant increase in body weight.

Effect on the Liver and Muscle

Administration of dexamethasone caused a significant effect on the liver and muscle of the experimental animals. However, phytochemical administration reversed some of these effects. Administration of 400 mg/kg body weight of *Ocimum gratissimum* reversed the depletion of liver glycogen caused by dexamethasone.[32] Livers of rats treated with *Ficus mollis* leaves had minimal inflammation compared to the animals administered with only dexamethasone.[37] The study conducted by Fofie *et al*.[38] revealed that the administration of Stem bark of *Ceiba pantandra* extract significantly reduced the dexamethasone-induced liver and cardiac hypertrophy. The extract also increased hepatic protein concentration and catalase activities.[38] Treatment of MS with *Sargassum angustifolium* caused a partial alleviation in the lipid accumulation and steatosis in the liver of the treated animals.[39] In the study of Kamani *et al*.,[40] *Emilia coccinea* significantly reduced the liver weight of the treated animals. The administration of aqueous and ethanol extract of *Oroxylum indicum* increased glycogen contents of the liver and muscle.[41]

Effect on Blood glucose level

The administration of Dexamethasone caused a significant elevation of the blood glucose level of the animals. However, in all the studies that assessed blood glucose, it was revealed that administration of the plant extracts despite the differences in the quantity and type of phytochemicals significantly caused a reduction in the blood glucose level.[17–19,21,22,24,25,31,33,38–40,42–48]

Effect on Lipid Content

The administration of Dexamethasone caused a significant elevation of total cholesterol, triglycerides, and low-density lipoprotein-cholesterol (LDL-C) levels while high-density lipoprotein-cholesterol (HDL-C) was reduced in the animals. However, in most of the studies that assessed the lipid profile, it was revealed that administration of plant extracts despite the differences in the quantity and type of medicinal plants, HDL-C was increased while cholesterol, triglycerides, and LDL-C were decreased.

However, there were some discrepancies in the findings of some studies. A study conducted by Okwuosa *et al*.[42] using Wistar rats revealed that *Pterocarpus santomiloides* aqueous leaf extract at 200 mg/kg significantly increased triglyceride concentration in the treated animals. Two studies in this review reported that *Allium affine* extract,[49] and high dose *Nepenthes khasiama*[50] showed no significant effect in reducing LDL-C levels. A study by Tamboli *et al*.[41] reported that aqueous and ethanolic extract of *Oroxylum indicum* did not affect triglyceride and total cholesterol levels.

Effect on blood pressure

Five out of the 34 studies included in this study assessed the impact of medicinal plants on blood pressure following the induction of hypertension through the administration of dexamethasone. The findings revealed that the medicinal plants used in these 5 studies were effective in reversing the adverse effects caused by dexamethasone administration. The plants were reported to significantly lower the systolic blood pressure in the treated animals.[20,27–30]

Findings from this review provide valuable insights into the complex interplay between glucocorticoid administration, metabolic dysregulation, and the potential mitigating effects of natural compounds.

The reviewed studies consistently demonstrated that dexamethasone is associated with the development of MS. Metabolic perturbations induced by dexamethasone included insulin resistance, dyslipidemia, hypertension, and abdominal obesity.

The potential remediation role of medicinal plants in mitigating dexamethasone-induced MS is a novel aspect addressed in this systematic review. This review revealed that the administration of dexamethasone significantly decreased the body weight of the experimental animals. This finding is consistent with the report of Aru *et al*.[52] which revealed that the treatment with dexamethasone led to significantly decreased body mass, lean body mass, and fat mass. The anorexic effect of dexamethasone was also demonstrated in rats, which led to a reduction in food intake and weight gain.[53] Dexamethasone is a glucocorticoid that inhibits the production of hypothalamic corticotropin-releasing hormone (CRH) thereby resulting in reduced body weight.[54-57]

Findings from this review also showed that some studies reported no effect or beneficial effect of the studied medicinal plants in reversing the effects of dexamethasone on the body weights of the animals. Studies have shown that the consumption of medicinal plants ameliorates metabolic syndrome through the regulation of metabolic pathways.[58] Other studies have also revealed the positive effects demonstrated by phytochemicals in the reduction of blood glucose levels, and blood pressure, and alleviation of various manifestations of metabolic syndrome like central obesity through the antioxidant activities of medicinal plants.[59,60] Phytoestrogen contained in some medicinal plants has been shown to counteract the cellular derailment responsible for the MS development through increased insulin sensitivity and downgrading of pro-inflammatory cytokines.[61]

Studies included in this review suggested that dexamethasone exerts its effects through multiple pathways including lipid metabolism, and modulation of insulin signaling, among others. One major pathway through which dexamethasone exerts its effects in the included studies is the elevation of blood glucose. This finding is consistent with several studies, among which is a study by Pasternak *et al*.,[62] which revealed a significantly elevated arterial blood glucose level following exposure to dexamethasone. Also, Martinez *et al*.[63] reported that dexamethasone administration led to increased glycemia among the experimental animals. Several studies in the review showed that the administration of dexamethasone-induced insulin resistance. This is in line with other studies that revealed the induction of insulin resistance by glucocorticoids.[64-66] The observed reversal of the detrimental effect of dexamethasone on metabolic variables by phytochemical administration further underscores their potency and possession of health-promoting benefits.[15]

Table 1A: Summary of the Included Studies (A: 2010-2014)

Studies	Year of publication	Plant	Animal characteristics	Quantity and route of administration of dexamethasone	Quantity and route of administration of the extract	Effect of the medicinal plant
[19]	2010	*Butea monosperma*	Swiss mice of either sex, weighing 25-30 g	Daily administration of Dexamethasone 1mg/kg body weight administered intramuscularly for 7 consecutive days	50,100,200mg/kg administered orally	1. *B. monosperma*-treated mice had significantly decreased levels of glucose, triglycerides, LDL, and VLDL. 2. Atrogenic Index and LPO were significantly reduced 3. Body weight gain was observed in the treated mice.
[42]	*2011*	*Pterocarpus santaniloides* leaf extracts	Male Wistar rats (100 -130 g)	10 mg/kg body administered subcutaneously	200 and 400 mg/kg of methanolic and aqueous extracts administered orally	1. The extracts reduce blood glucose. 2. Aqueous extract increases triglyceride level
[41]	*2011*	*Oroxylum indicum* (L.)	Male Wistar rats (150-200g)	10 mg/kg administered via subcutaneous	300 and 500 mg/kg aqueous and ethanolic extracts administered orally	Aqueous extract at low doses did not affect glycogen content. The high dose of aqueous and the two doses of ethanolic extracts significantly increased hepatic and muscle glycogen content. The extracts however did not have any effect on cholesterol and triglyceride levels
[17]	*2012*	*Gundelia tournefortii*	Male Swiss mice (24.6-33.2gram)	1 mg/kg administered Intramuscularly 22 days	75, 150, and 300mg/kg administered orally for 22 days	1. Did not reverse the significant decrease in body weight caused by dexamethasone.

						2. Caused a significant decrease in blood glucose, cholesterol, and triglyceride levels
[18]	*2012*	*Woodfordia fruticosa*	Swiss mice weighing 25-30 g	1 mg/kg, administered intramuscularly	100, 200, and 400 mg/kg administered orally for 15 days	All mice treated with *W. fruticosa* had significantly reduced levels of glucose, cholesterol, triglyceride, LDL, VLDL, and atherogenic index while body weight and HDL levels increased.
[37]	*2013*	*Ficus mollis* leaves	Wistar rats (175-200 g) of both male and female	10 mg/kg administered subcutaneously for 10 days	200 and 400 mg/kg administered orally for 10 days	Glucose, cholesterol, triglycerides, and LDL decreased while HDL increased in the *F. mollis-treated* rats. Hepatic inflammation was markedly reduced in the treated rats compared with the untreated while there was no visible inflammation in the pancreatic cells of the *F.mollis*-treated rats
[43]	2014	Stem of *Lasia spinosa*	Wistar Rats	10 mg/kg subcutaneously	200 & 400 mg/kg for 12 days	*L. spinosa*-treated rats had significantly reduced blood glucose.
[31]	*2014*	*Ichnocarpus frutescens* leaves	Male Wistar rats weighing about 200-250 g	3 mg/kg administered subcutaneously for 21 days	150 and 300 mg/kg administered orally for 14 days	The two doses caused a significant reduction in the fasting blood glucose levels
[44]	*2014*	*Nepenthes khasiana*	Wistar rats of either sex weighing 100 ± 20g	10 mg/kg for 10 days administered subcutaneously	250 & 500 mg/kg administered orally	The *N. Khasiana* significantly reduced the elevation in the serum glucose, cholesterol, triglyceride, and LDL while it increased HDL compared with the untreated group.

Table 1B: Summary of The Included Studies (B: 2015-2019)

Studies	Year of publication	Plant	Animal characteristics	Quantity and route of administration of dexamethasone	Quantity and route of administration of the extract	Effect of the medicinal plant
[26]	*2015*	*Moringa peregrina* (Forssk.) Fiori.	Male Wistar rats (200-250 g)	30 µg/kg administered subcutaneously for 14 days.	100, 200, and 400 mg/kg administered orally	*M. peregrina* prevented the rise in systolic blood pressure, augmented body weight loss, reduced plasma H_2O_2 concentration, and increased ferric reducing antioxidant power value
[50]	2015	Methanolic extract of *Syzygium alternifolium* (MESA)	Male and female Wistar rats (150-180g)	10 mg/kg administered subcutaneously for 8 days	100 and 200 mg/kg/day administered orally	The two doses of MESA reduced cholesterol, triglycerides, LDL, and VLDL while they increased HDL levels.
[28]	2015	Hydroalcoholic extract of *Ferula foetida* stems	Male Wistar rats (200 ± 20g)	30 µg/kg administered	200, 400, and 800 mg/kg administered	*F. foetida* extract significantly reduced Systolic blood pressure and increased plasma ferric

				subcutaneously for 14 days.	orally from the 8th day	reducing antioxidant power (FRAP) value.
[25]	*2016*	*Pterocarpus marsupium* and pioglitazone	Male Wistar rats	8 mg/kg administered intraperitoneally	1 and 2 g/kg of *Pterocarpus marsupium; and* 60 mg/kg of pioglitazone administered orally for 12 days	Treatment with ethanolic extract of *P. marsupium* and pioglitazone significantly reduced blood glucose and insulin. Homeostatic model assessment of insulin resistance (HOMA-IR) and insulin sensitivity (HOMA-IS) were also improved.
[27]	*2016*	*Kelussia odoratissima* Mozaff	Male Wistar rats (200 ± 20 g)	30 µg/kg administered subcutaneously for 14 days.	100, 200, and 400 mg/kg administered orally	1. Systolic blood pressure and plasma H_2O_2 concentration were significantly decreased *K. odoratissima*. Weight gain was significantly improved in the *K. odoratissima*-treated rats
[29]	*2017*	*Beta vulgaris*	Adult Wistar rats of either sex, weighting 150-200 g	Subcutaneous administration of 20 µg/kg for 14 days	100 and 300 mg/kg administered orally for 14 days	*B. vulgaris*-treated rats had significantly reduced heart rates compared with the untreated rats.
[35]	*2018*	*Moringa oleifera* Bark	Male Wistar rats initially weighing 180 – 200 g	1 mg/kg administered through intraperitoneal route (Acute study group), and subcutaneously (chronic study group)	15mg/kg petroleum ether fraction; 140 mg/kg Ethyl acetate fraction; or 95mg/kg Aqueous fraction administered orally	*Moringa oleifera* extracts did not prevent body weight loss while they significantly reduced hyperglycemia, hypertriglyceridemia, hyperinsulinemia, and HOMA IR.
[38]	2018	Stem Bark of *Ceiba pentandra*	Male and female Wistar rats (280-320g)	1 mg/kg administered intramuscularly for 8 days	75 and 150 mg/kg administered orally	Blood glucose and triglycerides were significantly reduced by *C. pentandra* Hepatic and cardiac hypertrophy were reduced in the treated groups Hepatic protein concentration and catalase activities were significantly increased.
[46]	*2019*	*Parkia biglobosa* extract	Male Wistar rats	1mg/kg administered Intramuscularly	25, 50, and 100 mg/kg administered for 14 days	There was significant hypoglycemia in groups treated with 100mg/kg of *P. biglobosa* extract
[33]	*2019*	*Baillonella toxisperma*	Wistar rats of both sexes (180–250 g)	intraperitoneal injection of 1 mg/kg for 8 days	60, 120, and 240 mg/kg administered orally	1. *B. toxisperma* did not have any effect on the body weight of the treated rats

						2. Blood glucose level was significantly reduced while markers of liver function were reduced in the blood of treated rats.
[47]	2019	Bark Extract of *Pinus eldarica*	Male Wistar rats (250±20g)	Subcutaneous injection of 10mg/kg for 7 days	100, 200, and 400 mg/kg administered intraperitoneally for 28 days	1. *P. eldarica* bark extract reduces blood glucose, triglycerides, and total cholesterol levels. 2. It increases plasma ferric-reducing antioxidant power value and reduces malondialdehyde and hydroperoxide levels 3. Hepatic Histopathological distortions induced by dexamethasone were reversed.

Table 1C: Summary of The Included Studies (C: 2020-2023)

Studies	Year of publication	Plant	Animal characteristics	Quantity and route of administration of dexamethasone	Quantity and route of administration of the extract	Effect of the medicinal plant
[36]	*2020*	*Cissus polyantha Gilg*	Male Wistar rats weighing between 220 and 250g	1 mg/kg administered Subcutaneously	Oral administration of 111, 222, and 444 mg/kg	*C. polyantha* increased body weights, glutathione levels, and activities of catalase and superoxide dismutase. Blood glucose, hyperlipidemia, serum insulin, insulin resistance index, and cardiovascular variables were significantly reduced in the *C. polyantha*-treated rats
[20]	*2021*	*Piper sarmentosum* Roxb. Leaves	Male Sprague Dawley rats aged 8-12 weeks and weighing (250-300g)	20 µg/kg administered subcutaneously for 28 days	500 mg/kg administered orally for 28 days	Treatment with *Piper sarmentosum* significantly reduced Mean Arterial Blood pressure, Systolic Blood pressure, and diastolic blood
[34]	2021	*Amaranthus spinosus*	Wistar rats of both sexes aged 12 weeks weighing between 170 to 260 g	Intraperitoneal administration of 10mg/kg for 8 days	High (500 mg/kg) and low (250 mg/kg) doses of ethanolic extracts for 8 days	1. Groups treated with the ethanolic extracts of the *A. spinosus* leaves showed a significant reduction in body weight.

						2. The levels of cholesterol and VLDL decreased while HDL increased in the treated groups.
[24]	*2021*	*Schumanniophyton magnificum* stem bark	Male Wistar rats weighing 170 g to 260 g	8 mg/kg, administered intraperitoneally	200 mg/kg and 400mg/kg for 11 days	*S. magnificum* reduced blood glucose, Aspartate aminotransferase (AST), and uric acid levels.
[32]	*2021*	*Ocimum gratissimum*	Male Wistar rats 130±20 g	1 mg/kg administered intraperitoneally for 10 days	400 mg/kg administered orally for 10 days	1. *O. gratissimum* did not affect body weight 2. The depletion in the liver glycogen was reversed in the group treated with the extract 3. There was an increase in the hexokinase activities in the group treated with the extract
[21]	2022	Methanolic Flower Head Extract of *Tagetes patula*	Sprague Dawley rats of either sex weighing 230–280 g	4 mg/kg, administered intraperitoneally	200 & 400 mg/kg, administered orally for 12 days	1. Decreased fasting blood glucose and insulin levels were observed in the *T. patula*-treated rats. 2. Insulin sensitivity was increased in the treated group.
[39]	*2022*	*Sargassum angustifolium*	Wistar male rats, 200-220 g	10 mg/kg administered subcutaneously for 7 days	20, 40 & 80 mg/kg orally for 7 days	1. Treatment with *S. angustifolium* significantly reduced levels of blood glucose, triglycerides, total cholesterol, LDL, and malonaldehyde level 2. Diffused steatosis and lipid accumulation observed in the dexamethasone-only group were partially alleviated in the *S. Angustifolium*-treated group.
[22]	2022	*Phoenix dactylifera* L. Seeds	Male Rabbits (0.77-1.5kg)	150 mg/kg administered intraperitoneally	200 & 400 mg/kg administered orally	*P. dactylifera* produced a dose-dependent reduction in blood glucose levels.
[40]	*2022*	*Emilia coccinea* aqueous extract	Male Wistar rats (180-250g)	1 mg/kg administered intraperitoneally for 8 days	107.5, 215 & 430 mg/kg administered orally	Blood glucose, cholesterol, triglycerides, LDL, and markers of liver functions were reduced significantly while HDL was increased by *E. coccinea*
[23]	*2022*	*Garcinia kola* Seeds	Wistar rats	4 mg/kg administered intravenously for 3 days	50 & 100 mg/kg administered orally for 14 days	*G. kola* significantly prevented the postprandial glycemia peak and reduced pancreatic cell abnormality.

[30]	*2022*	*Malus domestica* peel	Male and female Wistar rats (150-200g)	1.8 mg/kg administered subcutaneously once a week for 2 weeks	200 & 400 mg/kg administered orally for the 2 weeks	Blood pressure variables were significantly lowered in the *M. domestica*-treated rats.
[48]	*2023*	*Tapinanthus dodoneifolius*	Male Wistar rats weighing between 220 and 250 g	1 mg/kg administered subcutaneously for 10 days	125, 250, and 500 mg/kg	Blood glucose, cholesterol, triglycerides, LDL, and malondialdehyde were significantly reduced while reduced glutathione levels and activities of catalase and superoxide dismutase increased in the *T. dodoneifolius* treated dexamethasone-induced insulin-resistant rats.
[49]	*2023*	*Allium affine* Extract	Wistar rats	10 mg/kg administered subcutaneously for 10 days	50, 100, 200 & 400 mg/kg oral administration	Blood glucose, cholesterol, triglyceride, LDL, VLDL, Aspartate Aminotransferase, Alanine transaminase, and malondialdehyde levels were significantly reduced by *A. affine* treatment in the dexamethasone-exposed rats.

Conclusion

This systematic review provided a comprehensive overview of the role of medicinal plants in mitigating the effects caused by the administration of dexamethasone. In this study, dexamethasone caused detrimental effects on body functions such as elevated blood glucose level, weight loss, increased systolic blood pressure, and elevated triglyceride level. It was also revealed that the administration of medicinal plants reversed the negative effect of dexamethasone in the experimental animals. Therefore, there is a need to further investigate the interplay between medicinal plants and metabolic syndrome at the molecular and systemic levels.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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