Review Article

Preclinical updates of the homoeopathic medicines used in diabetes mellitus: A Narrative review

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Abstract

Introduction: Homoeopathy, one of the most commonly employed alternative medicines globally, has a wide range of role in the management of diabetes. Screening of the action of homoeopathic medicines in diabetes on animal model not only helps in validating their antidiabetic potential but also aids in understanding their effect on living systems and their mechanism of action. The present review focusses on the collection of results of pre-clinical studies carried out on homoeopathic medicines employed in the management of diabetes. **Methodology:** PubMed, HomBRex portal, and published literature such as library catalogue were searched up to November 2019. The search terms employed were 'Homoeopathy', 'Diabetes' and their MeSH variations in PubMed and in HomBrex search was made using the condition 'Diabetes'. **Results:** Fifteen studies were included in the review. Twenty medicines were evaluated for their antidiabetic efficacy either *in vivo* or *in vitro*. Most of the preclinical research on diabetes was carried out on *Syzygium jambolanum* and *Cephalandra indica* in mother tincture form and potencies, substantiating their effectiveness in the management of diabetes. Apart from the medicines discussed in the current review, there are many other medicines in Homoeopathy which are used to treat diabetes and these also should be validated scientifically for global acceptance by the scientific fraternity. **Conclusion:** Considering the hypoglycaemic potential, availability and cost-effectiveness of homoeopathic medicines, future research should focus on screening their effectiveness in the management of diabetic complications and other metabolic disorders.

Keywords: Diabetes, Homoeopathic medicine, Homoeopathy, *In vitro*, *In vivo*, Pre-clinical

Introduction

In the current global health scenario, diabetes mellitus (DM) is the most common endocrine disorder posing significant public health concern, producing substantial morbidity, mortality and long-term complications regardless of the latest advances in health care and management.[1] In the allopathic system of medicine, several orally administered drugs, recombinant drugs and genetically modified insulin are abundantly available in the market for the management of DM, which are reported to cause adverse effects.[2] The care of diabetic patients has been influenced by a growing interest in complementary and alternative medicine.[1]

Homoeopathy embraces a holistic approach in curing diverse diseases and it is used globally as an alternative medicine.[3] Homoeopathy seeks to cure in harmony with natural laws of healing. Potentized homoeopathic medicine, which undergoes a process of serial dilution along with succussion, is believed to retain properties of the original source substance. These homoeopathic medicines are employed in each case, on the basis of the homoeopathic principles, following the 'Law of similars'. Hydroalcoholic extract of the original drug substance termed as 'Mother tincture', which is prepared without potentisation is also used as a homoeopathic medicine.[4,5]

Homoeopathy is more effective in the management of Type II DM compared to Type I DM as, in the latter, insulin secretion

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is grossly affected due to damage of the beta cells of pancreas. Homoeopathic medicines can be given along with insulin therapy when beta cells of pancreas have not undergone a degenerative change.[6] The homoeopathic medicines for diabetes are depicted in Figure 1.[7]

Homoeopathic medicines are prepared following a well-defined procedure, starting from substances derived from the mineral, herbal, animal and energy sources.[8] Taking into consideration the growing interest of the public in homoeopathic system of medicine[9] and its cost-effectiveness, more research must be focused on screening these medicines for diabetes. This will help in scientifically establishing the effectiveness of homoeopathic medicines and may aid in attracting the global market for the manufacturing of such low-cost medicine which ultimately will come as a boon to financially weaker sections of the global population.

Over the past few years, there has been a rise in the number of preclinical (*in vitro* and *in vivo*) studies directed at assessing the efficacy of homoeopathic medicines in the management of diabetes and its complications[10] Thus, a review of literature of the pre-clinical studies was carried out to investigate homoeopathic medicines evaluated in the management of diabetes. The present review updates researchers regarding the work carried out to date in the area of pre-clinical screening of homoeopathic medicines for diabetes.

Methodology

Search strategy

The literature for the present review was identified using electronic databases including PubMed, HomBRex and published literature, like library catalogue. The reference lists of articles were also reviewed for additional relevant studies. Keywords used for this literature review include 'Homoeopathy', 'Diabetes' and their MeSH variations in PubMed and in HomBrex search was made using the condition 'Diabetes'. The search strategy was designed to include all the pre-clinical studies containing the descriptors that were published until November 2019.

Study selection

All titles, abstracts and complete articles were independently reviewed by two authors to eliminate duplications.

Inclusion criteria

In vitro and *in vivo studies* on homoeopathic medicines in the area of diabetes. Publications of the English language only were included.

Exclusion criteria

All the clinical studies were excluded. Review articles, Letters to the editor, conference proceedings and comments were also excluded. Unpublished data such as dissertations, data not published in peer-reviewed journals, and websites were not included.

Data extraction

Two authors independently extracted data on the medicines, dose, positive control, duration of study, outcome, results in *in vivo* studies and medicines, study assay, the outcome in *in vitro* studies. Discrepancies were resolved between authors by mutual consensus.

Results

The database search was carried out to find relevant scientific papers published up to November 2019 reporting original

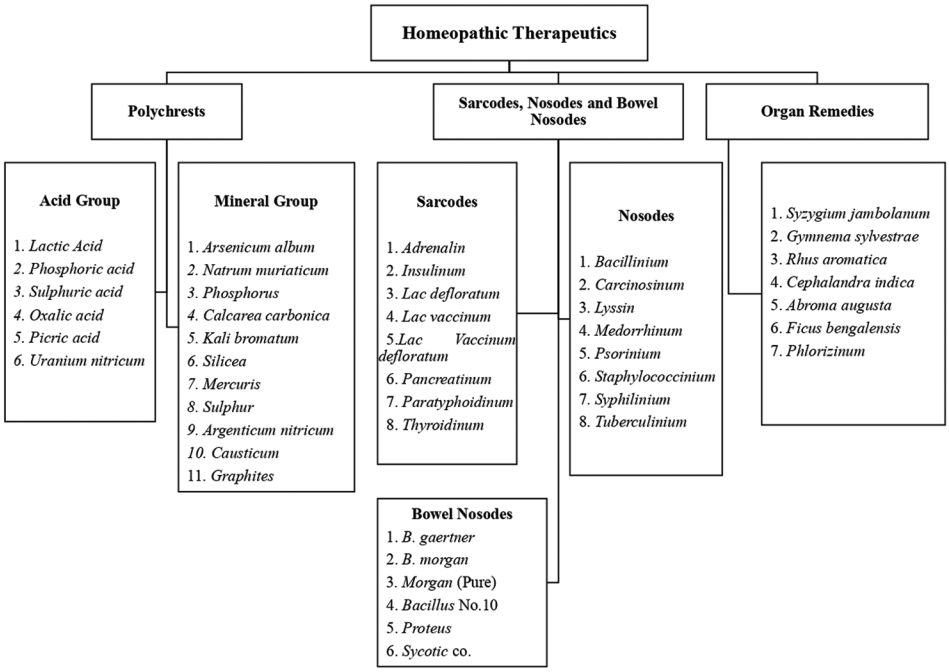

Figure 1: Commonly employed homeopathic therapeutics in the management of diabetes

pre-clinical research on homoeopathic medicines in the area of diabetes. The database search yielded 80 records, of which 77 were identified after the removal of duplicates. Of these, 30 review articles, 28 clinical studies and 4 commentaries were excluded as per the exclusion crieteria. After exclusion, 15 studies, consisting of 12 *in vivo* and 3 *in vitro* studies, were included for the present review [Figure 2]. No studies found were from outside India.

Preclinical research work was carried out on Homoeopathic medicines, namely *Syzygium jambolanum, Cephalandra indica, Gymnema sylvestre, Abroma augusta, Momordica charantia, Pterocarpus marsupium, Absinthium*/*Resina laricis, Chionanthus virginica, Uranium nitricum, Achilea millefolium*, *Allium sativum*, *Atropa belladonna*, *Cinchona officinalis*, *Hamamelis virginiana*, *Pulsatilla nigrican*, *Rhus toxidendron*, *Strychnos Nux-vomic, Iodium, Phosphorous and Alloxan.* The *in vivo* studies are summarised in Table 1 and *in vitro* studies in Table 2.

Syzygium jambolanum

Syzygium jambolanum Q is prepared from coarse powder of seeds of the plant containing 82.0%–86.0% v/v alcohol.[11] *Syzygium jambolanum* has been screened for its antidiabetic potential in mother tincture and potentised dilutions. Maiti *et al*. had evaluated the effect of *Syzygium jambolanum* Q on carbohydrate and lipid metabolic disorders in Streptozotocin (STZ)-induced diabetic male rats.[12,13] The results of the study indicated that *Syzygium jambolanum* Q treatment has a therapeutic effect on carbohydrate and lipid metabolic disorders and oxidative injuries in diabetic rats. *Syzygium jambolanum* Q has been found to decrease levels of blood glucose, triglycerides, total cholesterol, low-density lipoprotein cholesterol (LDLc), very low-density lipoprotein cholesterol (VLDLc), serum urea, serum creatinine, serum uric acid and serum albumin in diabetic rats. It was found to increase body weight, plasma insulin, liver and skeletal muscle glycogen, hepatic and renal catalase, peroxidase and superoxide dismutase (SOD) levels. The *Syzygium jambolanum* Q has also been found out to improve carbohydrate metabolic key enzyme activities in hepatic tissue i.e., hexokinase, glucose-6-phosphate dehydrogenase and glucose 6-phosphatase in diabetic rats. This work also showed that *Syzygium jambolanum Q* treatment decreases serum glutamate oxaloacetate transferase and serum

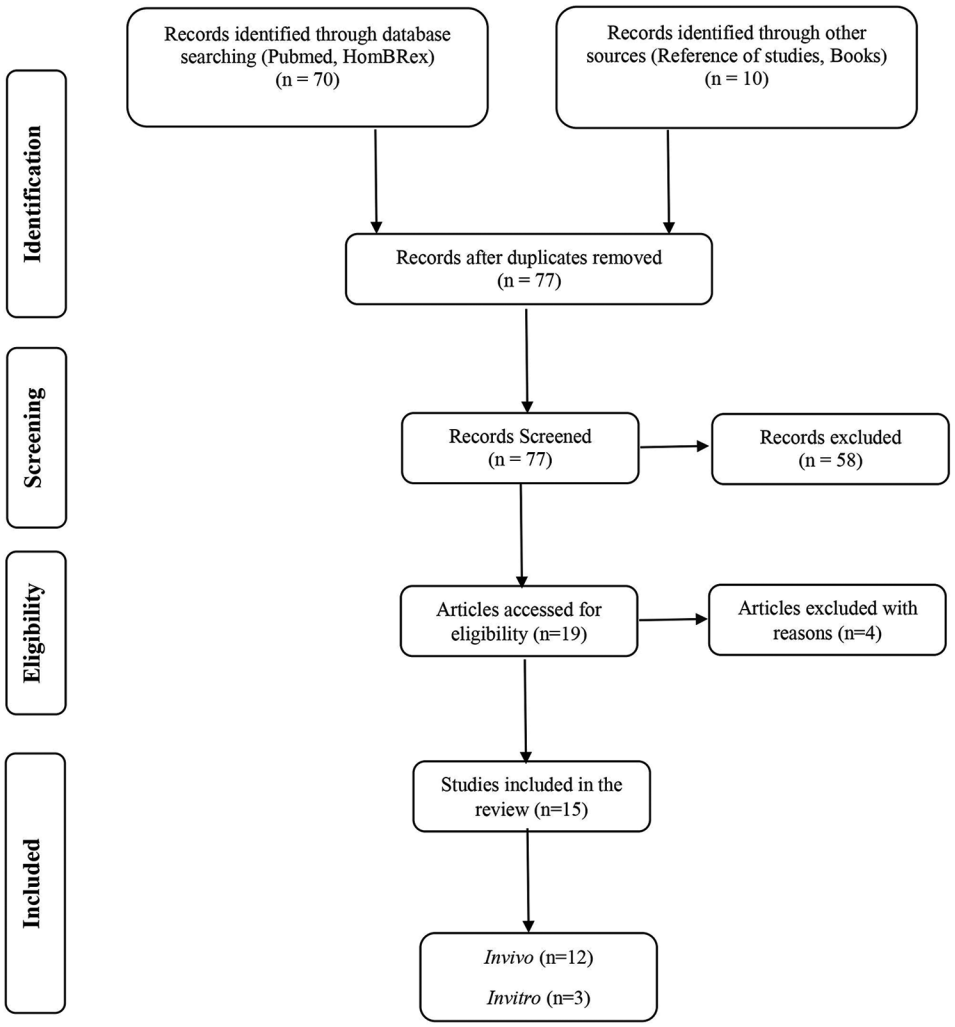

Figure 2: Study flow diagram

Table 1: Summary of in vivo pre-clinical studies of homoeopathic medicines in the management of diabetes

Authors (years)	Target	Medicine(s) evaluated	Positive control	Q/P	Dose/day	Treatment duration (days)	Outcome
Maiti *et al*., (2013)[12]	Streptozotocin induced diabetic rat	*Syzygium jambolanum*	NA	Q	60 µl/100 gm body weight orally twice a day	40	↓Fasting blood glucose levels
Maiti *et al*., (2014)[13]	Streptozotocin induced diabetic rat	*Syzygium jambolanum*	Glibenclamide 60 mg/kg body weight	Q	60 µl/100 gm body weight orally twice a day	40	↓Fasting blood glucose levels
Sathish *et al*., (2013)[14]	High fat diet and high fructose diet followed by Streptozotocin induced diabetic rats	*Syzygium Jambolanum, Cephalandra indica*	Metformin, 50 mg/kg body weight	Q, 6C, 30C	20 µl/100 g body weight, twice daily orally	30	↓Fasting blood glucose levels
Gupta (2013)[16]	Alloxan induced diabetic albino rats	*Cephalandra indica* and *Absinthium D1/Resina laricis D3*	NA	Q	25 µl, 50 µl 75 µl/100 g body weight orally	21	↓Blood glucose levels
		Abroma augusta	NA	Q	25 µl, 50 µl 75 µl/100 g body weight orally	21	Mild hypoglycaemic activity and no stabilisation of blood glucose levels
Rastogi *et al*., (1988)[17]	Alloxan induced diabetic rats	*Cephalendra indica*	Glibenclamide Tolbutamide Insulin	Q	25 µl, 50 µl 75 µl/100 g body weight orally	45	↓Blood glucose levels
Kapoor (2016)[18]	Alloxan induced diabetic rabbits	*Pterocarpus marsupium* *Cephalandra indica* *Momordica charantia* *Chionanthus virginica* *Uranium nitricum*	NA	Q, 3X, 6X	15 µl/100 g body weight orally	NA	↓Blood glucose levels
		Bryonia alba, gymnema, sylvestre, iodium, phosphorous		Q, 3X, 6X	15 µl/100 g body weight orally	NA	No change in blood sugar levels
Pal *et al*., (2013)[19]	Streptozotocin induced diabetic rat	*Cephalandra indica*	Glibenclamide 1 mg/kg body weight	Q, 6C, 24X, 12C, 30C	75 µl/100 gm body weight orally	21	↓Blood glucose levels
Kishore and Singh (2017)[20]	Streptozotocin induced diabetic neuropathic rat	*Cephalendra indica*	Gabapentin 30 mg/kg body weight	Q, 6 C 30 C	200 µl/100 g body weight orally	90	↓Serum blood glucose levels, neuropathic pain
Kishore and Singh, (2019)[21]	Streptozotocin induced diabetic nephropathic rat	*Cephalendra indica*	Glimepride 10 mg/kg	Q, 6 C 30 C	200 µl/100 g body weight orally	75	↓Fasting blood glucose levels↑Renal function
Kishore and Singh, (2017)[23]	Streptozotocin induced diabetic nephropathic rat	*Gymnema sylvestre*	Glimepride 10 mg/kg	Q, 6 C 30 C	200 µl/100 g body weight orally given in divided doses thrice daily	75	↓Fasting blood glucose levels↑Renal function
Giri, (2017)[24]	Alloxan induced hyperglycaemic rabbits	*Momordica charantia*	NA	Q	20 µl/100 g body weight orally	30	↓Blood glucose levels
Kumar and Nayak, (2008)[25]	Alloxan induced diabetic rats	Alloxan	NA	6X, 30X, 200X, 1000X	50 µl/100 g body weight orally	30	↓Blood glucose levels↑Growth hormone levels

Q: Mother tincture, P: Potencies, NA: Not available, C: Centesimal potency, X: Decimal potency

Table 2: Summary of *in vitro* pre-clinical studies of homoeopathic medicines in the management of diabetes

Authors (years)	Medicine(s) evaluated	Q/P	Study assays	Outcome
Rashmi *et al*., (2015)[15]	*Syzygium jambolanum* *Cephalandra Indica*	Q, 30C, 200C	Invitro albumin glycation Hemolysis test Intracellular antioxidant activity of erythrocytes	Anti-glycation activity cell protection ability
Kishore and Singh, (2015)[22]	*Gymnema sylvestre*	Q, 6C and 30C	In vitro anti-glycation activity using BSA Erythrocyte sorbitol accumulation inhibition assay Aldose reductase enzyme inhibition	Inhibition of AGE's Inhibition of erythrocyte sorbitol accumulation Inhibition of aldose reductase enzyme
Rehman *et al*., (2018)[26]	*Achilea millefolium* *Allium sativum* *Atropa belladonna* *Cinchona officinalis* *Hamamelis virginiana* *Pulsatilla nigrican* *Rhus toxidendron* *Strychnos Nux-vomica*	Q	Alpha-glucosidase inhibitory activity	Good activity - Strychnos Nux-vomica, Atropa belladonna Moderate activity - Rhus toxidendron, Hamamelis. virginiana, Achilea. millefolium and Pulsatilla nigricans Weak activity - Allium sativum and Cinchona officinalis

Q: Mother tincture, P: Potencies, C: Centesimal potency, AGE's: Advanced glycation end products, BSA: Bovine serum albumin

glutamate pyruvate transferase levels, thereby attenuating diabetes-induced hepatic injury in rats.

Another study elucidated the molecular mechanism of *Syzygium jambolanum* Q and its 6C and 30C potencies using a rat model of high fat and high fructose-induced Type 2 diabetes. *Syzygium jambolanum* Q and its 6C, 30C potencies exhibited antidiabetic effects, improving insulin levels and acting through activation of insulin signaling molecules (insulin receptor [IR], v-akt murine thymoma viral oncogene homologue [Akt], p-Akt^{ser473} and glucose transporter-4 [GLUT4] proteins) in skeletal muscle of Type 2 diabetic rats. Variations were observed between SJMT and its potencies in the expression of insulin signaling molecules; however, ultra-molecular 30C dilution was the most effective in reducing fasting blood glucose.[14]

Increased glycation of proteins and accumulation of advanced glycation end products (AGEs) have been implicated in the pathogenesis of diabetic complications. In this respect, Rashmi *et al*. evaluated the effectiveness of *Syzygium jambolanum* Q, 30C and 200C in preventing glycation-induced structural modifications in albumin and their cellular protection ability in human erythrocytes *in vitro*. *Syzygium jambolanum* Q, 30Cand 200C inhibited glycation of albumin as evident from decreased levels of fructosamines, protein carbonyls, bound glucose and also protected thiol groups of albumin from oxidation. The medicine found to scavenge erythrocytes from glycation-induced oxidative stress and preventing free radical-induced erythrocytes membrane peroxidation which may have led to increased membrane rigidity, decreased cellular deformability, reduced erythrocyte survivaland lipid fluidity. The effects were much prominent with *Syzygium jambolanum* Q than compared to 30C and 200C.[15]

Cephalandra indica

Cephalandra indica Q is prepared from fresh pulp and leaves of the plant in 40.0% v/v alcohol.[11] Apart from *Syzygium jambolanum*, *Cephalandra indica* is also well used in homoeopathic system of medicine in the management of diabetes. In two studies, Rastogi *et al*. initially screened the hypoglycaemic potential of *Cephalandra indica* Q in alloxan-induced diabetic rats.[16,17] The experimental studies revealed that regular administration of *Cephalandra indica Q* caused noticeable hypoglycaemic activity at a microdose level ranging from 25 to 75 µl/100 g. body weight and histopathological studies revealed the regeneration of pancreatic beta cells. Further, investigation of hypoglycaemic activity in alloxan induced diabetic rabbits was carried out and results revealed that *Cephalandra indica Q* and it's 3X preparations show a prominent drop in blood sugar levels.[18] Pal *et al*. had evaluated the antidiabetic effect of *Cephalandra indica Q* in STZ-induced diabetic rats at a dose of 75 µl/100 g. body weight and found a significant reduction in blood glucose levels, regain of body weight, recovery of beta-cells in the pancreas and partial recovery hepatic tissue of the *Cephalandra indica* Q-treated rats.[19]

Sathish *et al*. explained the molecular mechanism of *Cephalandra indica* Q and its 6C and 30C potencies by studying their effects on gastrocnemius muscle (Skeletal muscle) of high fat and high fructose-induced type-2 diabetic rats.[14] *Cephalandra indica* Q and its 6C, 30C potencies showed hypoglycaemic effect, restored insulin and lipid levels to normal levels. In gastrocnemius muscle of diabetic rats, these preparations improved insulin sensitivity by augmenting IR, v-akt murine thymoma viral oncogene homologue (Akt), p-Aktser473 and glucose transporter-4 (GLUT4) proteins. The effects were more prominent with 6C and 30C preparations compared to *Cephalandra indica Q*.

Glycation and AGEs formation accompanied by the formation of free radicals through auto-oxidation of glucose and glycated proteins leads to microvascular and macrovascular complications of diabetes. *Cephalandra indica Q*, 30C and 200C preparations were evaluated for their effectiveness

in inhibiting glycation-induced structural modifications on protein albumin and their protective effect on human erythrocytes *in vitro*. The antiglycation potential of *Cephlandra indica* was manifested with reduced levels of fructosamines, protein carbonyls and bound glucose which are normally increased during albumin glycation. *Cephalandra indica* Q showed the highest efficacy when compared to 30C and 200C for antiglycation potential. The preparations also protected free thiol and amino groups of albumin from oxidation-inhibiting glycation. These *Cephalandra indica* Q and diluted preparations protected erythrocytes from haemolysis and also antioxidant power of erythrocytes was increased as evidenced by a rise in ferric-reducing ability of plasma activity. Erythrocyte protection was maximum with 200C dilution of *Cephalandra indica*.[15]

Kishore and Singh screened *Cephalandra indica Q*, 6C, and 30C potencies in the management of diabetic neuropathic pain and nephropathy in STZ-induced diabetic rats.[20,21] *Cephalandra indica* Q and 6C and 30C potencies increased pain threshold and improved motor nerve conduction velocity in rats experiencing neuropathy. In rats suffering from nephropathy, *Cephalandra indica Q*, 6C and 30C increased body weight, serum insulin levels, HDLc and decreased fasting blood glucose, urea, uric acid, creatinine, LDLc and VLDLc. Further, oxidative stress in sciatic nerve and kidneys was found to be significantly reduced as evidenced by improvement in SOD, reduced glutathione (GSH) and lipid peroxide levels. AGE's levels were also decreased in sciatic nerve and kidneys of rats treated with the preparations. Histopathology of kidneys indicates a structural improvement in nephrons by the action of *Cephalandra indica Q*, 6C and 30C. The studies conclude that *Cephalandra indica Q*, 6C and 30C confer a protective effect against diabetic nephropathy and neuropathic pain through inhibition of oxidative stress and AGEs. The effects were more pronounced with 30C dilution compared to *Cephalandra indica* Q and 6C dilutions.

Gymnema sylvestre

Gymnema sylvestre Q is prepared from coarse powder of leaves of the plant containing 76.0%–80.0% v/v alcohol.[11] Kishore and Singh reported that *Gymnema sylvestre* mother tincture, 6C and 30C preparations had potent antiglycation activity *in vitro*. The preparations were found to act by inhibiting AGEs formation, sorbitol accumulation and aldose reductase enzyme.[22] The same preparations were then evaluated for their role in attenuating diabetic nephropathy in STZ-induced diabetic rats *in vivo*.[23] In diabetic animals, there were increases in fasting blood glucose, urea, uric acid, creatinine, blood urea nitrogen, total cholesterol, triglycerides, low-density lipoproteins and very low-density lipoproteins with a reduction in high-density lipoproteins. *Gymnema sylvestre* Q, 6C and 30C preparations improved the lipid profile, renal profile and fasting blood glucose in diabetic animals. Moreover, these preparations also restored the depleted antioxidant enzymes such as SOD, GSH and catalase in diabetic nephropathic rats. The AGEs level was also reduced by these preparations in kidneys and histopathological data indicates that structural changes induced by STZ in kidneys, liver and pancreas were reversed by these preparations. Amongst the preparations, 30C dilution was found to be more effective, and effects were comparable to Glimipride, in attenuating diabetic nephropathy in STZ rats.

Abroma augusta

Abroma augusta Q is prepared from the moist leaves of the plant and contains 42.0%–46.0% v/v alcohol.[11] Rastogi *et al*. reported that *Abroma augusta* Qhas mild hypoglycaemic potential at doses of 50 µl, 75 µl and 0.1 ml/100 g. b.w. in alloxan-induced diabetic rats without stabilisation of blood glucose levels.[16]

Momordica charantia

Momordica charantia Q is prepared from fresh pulp of the fruits of the plant in 57.0% v/v alcohol.[11] Sundaram studied the effects of *Momordica charantia Q* on blood sugar, serum growth hormone and prolactin levels in alloxan-induced hyperglycaemic rabbits. The report indicates that *Momordica charantia Q* at a dose of 20 µl/100 g body weight had significantly decreased blood sugar while increasing growth hormone and prolactin levels in diabetic rabbits.[24]

Absinthium X/*Resina laricis* 3X

Absinthium Q is prepared from coarse powder of leaves, seeds of the *Artemisia absinthium* in 63.0%–67.0% v/v alcohol. *Resina laricis* mother tincture is prepared from a highly viscous resin obtained by drilling trunks of Larix decidua.[11] *Absinthium* X/*Resina laricis* 3X formulation was found to exhibit perceptible hypoglycaemic activity at a microdose level ranging from 25 to 75 µl/100 g. body weight in alloxan-induced diabetic rats.[16]

Chionanthus virginica

Chionanthus virginica Q is prepared from coarse powder of bark of the plant and contains 61.0%–63.0% v/v alcohol.[11] *Chionanthus virginica* Q at a dose of 15 µl/100 g body weight was found to exhibit a decrease in blood sugar levels in alloxan-induced hyperglycaemic rabbits.[18]

Pterocarpus marsupium

Sundaram found that *Pterocarpus marsupium Q* and 3X preparations at a dose of 15 µl/100 g body weight significantly decreased blood glucose in alloxan-induced diabetic rats.[18]

Uranium nitricum

Uranium nitricum stock solution is prepared from *Uranium nitricum*, yellow-colored crystals with green fluorescence and contains 90% v/v alcohol.[11] *Uranium nitricum* 3X and 6X preparations were reported of showing hypoglycaemic activity at a dose of 15 µl/100 g body weight in alloxan-induced hyperglycaemic rabbits.[18]

Alloxan

Alloxan stock solution is prepared from anhydrous and orthorhombic crystals of alloxan.[11] A study evlauted dynamised and undynamised alloxan in 6X, 30X, 200X and 1000X potencies for its hypoglycaemic activity using

alloxan-induced diabetic albino rats.[25] Results indicated that dynamised alloxan in 6X, 30X, 200X and 1000X potencies decreased blood sugar levels along with an increase in growth hormone levels in diabetic rats compared to undynamised alloxan at same potencies. Hypoglycaemic activity of dynamised alloxan was attributed to reactivation/restoration of beta cells by acting through hypothalamo–hypophysial–pancreatic beta cells axis as evidenced from histological analysis of brain and pancreas of diabetic rats. Animals were even found to show stabilization of blood sugar levels even after withdrawal of dynamised alloxan in 30X, 200X and 1000X potencies for 10–25 days after completion of treatment period (30 days). Dynamised alloxan at 200X and 1000X potencies had shown a significant antidiabetic effect compared to 6X and 30X potencies.

In vitro alpha-glucosidase inhibitory activity of Homoeopathic mother tinctures

Rehman *et al*. had investigated the *in vitro* alpha-glucosidase inhibitory activity of eight homoeopathic medicines *Achilea millefolium*, *Allium sativum*, *Atropa belladonna*, *Cinchona officinalis*, *Hamamelis virginiana*, *Pulsatilla nigrican*, *Rhus toxidendron* and *Strychnos Nux vomica* in mother tincture form. Results indicated that *Strychnos Nux vomica* and *Atropa belladonna* showed the highest activity even greater than positive control and the effect was correlated to the presence of secondary metabolites such as alkaloids and flavonoids in these medicines. *Rhus toxidendron* and *Hamamelis virginiana* showed moderate inhibition and other mother tinctures were not able to inhibit α-glucosidase up to 50% and so were considered to be weak inhibitors.[26]

Discussion

The present review highlights that many medicines are employed in the homoeopathic system of medicine for the management of diabetes, but a few medicines have had their usage scientifically corroborated. Amongst these medicines, most of the preclinical research in diabetes in the past decade was carried out on *Syzygium jambolanum* and *Cephalandra indica* in mother tincture and potency formulations. These medicines have shown efficacy in reducing blood sugar levels, protecting beta cell destruction, restoring insulin levels, inhibiting the formation of AGEs and their probable molecular mechanism of action has also been elucidated. Apart from these two medicines, other medicines that have been evaluated earlier need to be revaluated for their antidiabetic potential as the earlier studies lack robust study protocols, comparison with a standard drug and histopathological evidences, etc.

In the above-reviewed studies, the rationale for the selection of the dose(s) of the medicines at which their efficacy was evaluated was not described. Moreover, some of the researchers had diluted mother tinctures and potencies in water before administration,[12,13,21,23] while a few had used undiluted medicines,[14,16,17,18,20,24] and the justification for the same was not stated in any of the reviewed papers. Keeping in view of the above points, further research should be carried out to address the above dissimilarities in animal models, and the results should be made open to biomedical researchers for bringing out uniformity in preclinical homoeopathic research.

Considering the small number of studies carried out, more pharmacological investigations (*in vivo* or *in vitro)* assuring their antidiabetic effect, the underlying mechanisms of action, long-term safety and potential toxicological effects are necessary to substantiate their appropriate use in humans. Most of these medicines are clinically employed in potentised forms i.e., in 6C, 30C and 200C, etc., and there is an ambiguity regarding their efficacy amongst the scientific fraternity. Hence, scientifically controlled studies devoted to potentised forms in investigating their mechanism and efficacy are encouraged. Moreover, these studies should report not only the magnitude of the effects but also the potential side effects and long-term safety.

In the reviewed studies, microvascular complications of diabetes such as neuropathic pain and nephropathy, respectively, were shown to be reduced by *Cephalandra indica* medicine in an animal model,[20,21] and nephropathy was found to be ameliorated by *Gymnema sylvestre* in diabetic rats.[23] Hence, screening of other homoeopathic medicines having hypoglycaemic activity in the management of diabetic complications including both microvascular and macrovascular should be the prime motive of future research. As these medicines have effectively shown to combat DM, these may be effective in the treatment of other metabolic disorders such as obesity and hyperlipidaemia, and hence screening of these medicines in the management/treatment of these disorders seems encouraging.

Most of the homoeopathic medicines discussed in this review are derived from plants and it is noteworthy that the hypoglycaemic effect of plant-derived medicines can interfere with allopathic hypoglycaemic drugs and insulin, which are standard treatments for diabetic patients.[27] Most physicians counsel their patients to avoid herbal medicine, but in some cases, the diabetic patients take it without informing their physicians. This type of therapy may lead to drug interaction or false and unstable blood glucose level monitoring.[28] Therefore, studies assessing the effect of homoeopathic medicines when given along with allopathic medicines in animal models of diabetes are encouraging and may provide valuable information on potential toxicities or possible herb–drug interactions or significant risks.

Many *in vitro* methods based on chemicals, isolated organs, cells and membranes are available to study the safety and efficacy of medicines in the management of diabetes.[29-33] These assays provide a platform for rapid screening of medicines and also may help in understanding the cellular and molecular effects of drugs which may substantiate their efficacy when screened in animal models. Hence, given the handful number of homoeopathic medicines available for the management of diabetes, applying the *in vitro* models will help in the swift analysis of these medicines for their efficacy.

Conclusion

The present review provides the researchers with an updated information on the status of pre-clinical antidiabetic research carried out on homoeopathic medicines and can guide them in planning future studies. Reproducibility of effects in basic pre-clinical research has the utmost importance and future antidiabetic studies may be planned as multiinstitutional, controlled, blinded studies to ensure quality and reproducibility in the evaluations carried out.

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Conflicts of interest

None declared.

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मधुमेह में इस्तेमाल होने वाली होम्योपैथिक दवाओं का पूर्वनैदानिक अद्यतनीकरण : एक विवरणात्मक निरीक्षण

प्रस्तावना : होम्योपैथी, जो वैष्विक तौर पर सबसे ज्यादा इस्तेमाल होने वाली वैकल्पिक चिकित्सा पद्धति है उसके मधुमेह प्रबंधन में व्यापक हस्तक्षेप हैं। मधुमेह के जीव प्रतिमानों में होम्योपैथिक दवाओं की कार्यवाही के परीक्षण ने न केवल उनकी मधुमेह–रोधी क्षमता को वैधता प्रदान करने में मदद की है बल्कि जीविका प्रणालियों और उनकी कार्यवाहक–क्रियाविधि पर इन दवाओं के प्रभावों को समझने में भी सहायता की है। मौजूदा निरीक्षण का केन्द्र मधुमेह के प्रबंधन में इस्तेमाल की गई होम्योपैथिक दवाओं पर किए गए ''प्राक''–नैदानिक अध्ययनों के परिणामों को इकट्ठा करने पर है। **प्रणालियाँ :** पबमेड, होमब्रेक्स पटल को नवंबर 2019 तक खोजा गया था। ''होम्योपैथी'', ''मधुमेह'' जैसे षब्दों और उनके एमईएसएच रूपांतरों को प्रयुक्त करके खोजा गया था। **परिणाम :** निरीक्षण में 14 अध्ययनों को समाहित किया गया था। 19 दवाओं को उनके मधुमेह–रोधी प्रभावोत्पादकता इन विवो या इन विट्रो के लिए मूल्यांकित किया गया था। मधुमेह के अधिकतर प्राक्–नैदानिक अनुसंधान को मूल अपमिश्रक में सिज़ीजियम जैबोलानम और सेफलेन्ड्रा इंडिका पर तथा मधुमेह के प्रबंधन में उनकी प्रभावकारिता को प्रमाणित करने वाली क्षमता पर कार्यान्वित किया गया था। मौजूदा निरीक्षण में वर्णित दवाओं के अतिरिक्त, ऐसी कई अन्य होम्योपैथिक दवाऐं हैं जिन्हें मधुमेह के उपचार में इस्तेमाल किया जाता है तथा जिन्हें वैज्ञानिक बिरादरी द्व ारा वैष्विक स्वीकार्यता के लिए वैज्ञानिक तौर पर प्रमाणित किया जाना अपेक्षित है। **निष्कर्ष :** होम्योपैथिक दवाओं की हाइपोग्लाइकेमिक क्षमता, उपलब्ध ाता और किफायत को ध्यान में रखते हुए, भविश्यगामी अनुसंधान का केन्द्र मधुमेह की समस्याओं और अन्य चयापचय विकारों के प्रबंधन में उनकी प्रभावकारिता को जांचने पर होना चाहिए।

Mises à jour précliniques des médicaments homéopathiques utilisés dans le traitement du diabète - une revue narrative

Le Introduction: L'homéopathie, l'une des médecines alternatives les plus couramment utilisées dans le monde, a un large éventail d'interventions dans la gestion du diabète. Le dépistage de l'action des médicaments homéopathiques dans des modèles animaux de diabète permet non seulement de valider leur potentiel antidiabétique, mais aussi de comprendre les effets de ces médicaments sur les systèmes vivants et leur mécanisme d'action. Le présent examen se concentre sur la collecte des résultats des études précliniques menées sur les médicaments homéopathiques utilisés dans la gestion du diabète. **Les méthodes :** PubMed, le portail HomBRex ont fait l'objet de recherches jusqu'en novembre 2019. Les termes de recherche utilisés étaient "Homéopathie", "Diabète" et leurs variantes MeSH. **Résultats :** Quatorze études ont été incluses dans l'examen. Dix-neuf médicaments ont été évalués pour leur efficacité antidiabétique in vivo ou in vitro. La plupart des recherches précliniques sur le diabète ont été menées sur Syzygium jambolanum et Cephalandra indica dans la teinture mère et dans des puissances qui confirment leur efficacité dans la gestion du diabète. Outre les médicaments examinés dans la présente étude, il existe de nombreux autres médicaments homéopathiques utilisés pour traiter le diabète qui doivent être validés scientifiquement pour être acceptés par la communauté scientifique au niveau mondial. **Le Conclusion:** Compte tenu du potentiel hypoglycémique, de la disponibilité et du rapport coût-efficacité des médicaments homéopathiques, les recherches futures devraient se concentrer sur le dépistage de leur efficacité dans la gestion des complications diabétiques et d'autres troubles métaboliques.

Actualizaciones preclínicas de los medicamentos homeopáticos usados en la diabetes – Una revisión narrativa

Introducción: Homoeopatía, uno de los medicamentos alternativos más comúnmente empleados a nivel mundial tiene una amplia gama de intervenciones en el manejo de la diabetes. La detección de la acción de los medicamentos homoeopáticos en modelos animales de diabetes no sólo ayuda a validar su potencial antidiabético, sino que también ayuda a comprender los efectos de estos medicamentos en los sistemas vivos y su mecanismo de acción. La presente revisión se centra en la recopilación de resultados de estudios preclínicos realizados sobre medicamentos homeopáticos empleados en el tratamiento de la diabetes. **Métodos:** PubMed, HomBRex portal fueron buscados hasta noviembre de 2019. Los términos de búsqueda empleados eran "Homoeopatía", "Diabetes" y sus variaciones de MeSH. **Resultados:** Se incluyeron catorce estudios en la revisión. Diecinueve medicamentos fueron evaluados para su eficacia antidiabética ya sea in vivo o in vitro. La mayor parte de las investigaciones preclínicas sobre la diabetes se realizaron en Syzygium jambolanum y Cephalandra indica en tintura materna y en potencias que corroboran su eficacia en el manejo de la diabetes. Aparte de los medicamentos discutidos en la revisión actual, hay muchos otros medicamentos de homeopatía que se utilizan para tratar la diabetes que necesitan ser validados científicamente para la aceptación global por la fraternidad científica. **Conclusión:** Considerando el potencial hipoglucémico, la disponibilidad y la rentabilidad de los medicamentos homeopáticos, la investigación futura debe centrarse en la evaluación de su eficacia en el tratamiento de las complicaciones diabéticas y otros trastornos metabólicos.

Präklinische Updates der homöopathischen Arzneimittel bei Diabetes-Eine narrative Überprüfung

Einführung: Die Homöopathie, eines der weltweit am häufigsten verwendeten Alternativmedikamente, verfügt über eine breite Palette von Eingriffen in die Behandlung von Diabetes. Das Screening der Wirkung homöopathischer Arzneimittel in Tiermodellen von Diabetes hilft nicht nur bei der Validierung ihres antidiabetischen Potenzials, sondern hilft auch, die Auswirkungen dieser Arzneimittel auf lebende Systeme und ihren Wirkungsmechanismus zu verstehen. Die gegenwärtige überprüfung konzentriert sich auf die Sammlung der Ergebnisse der präklinischen Studien, die auf die Homöopathischen Medikamente eingesetzt, die in das management von diabetes. **Methoden:** PubMed, HomBRex Portal wurden bis November 2019 durchsucht. Die verwendeten Suchbegriffe waren "Homöopathie", "Diabetes" und ihre Netzvariationen. **Ergebnisse:** Vierzehn Studien wurden in die überprüfung einbezogen. Neunzehn Arzneimittel wurden entweder in vivo oder in vitro auf ihre antidiabetische Wirksamkeit untersucht. Die meisten präklinischen Untersuchungen zu Diabetes wurden an Syzygium jambolanum und Cephalandra indica in Urtinktur und in Potenzen durchgeführt, die ihre Wirksamkeit bei der Behandlung von Diabetes belegen. Abgesehen von den in der aktuellen Überprüfung diskutierten Arzneimitteln gibt es viele andere Homöopathie-Arzneimittel, die zur Behandlung von Diabetes verwendet werden und wissenschaftlich validiert werden müssen, um von der wissenschaftlichen Gemeinschaft global akzeptiert zu werden. **Schlussfolgerung:** In Anbetracht des hypoglykämischen Potenzials, der Verfügbarkeit und der Kostenwirksamkeit homöopathischer Arzneimittel sollte sich die zukünftige Forschung auf das Screening ihrer Wirksamkeit bei der Behandlung diabetischer Komplikationen und anderer Stoffwechselstörungen konzentrieren.

糖尿病顺势疗法药物的临床前更新-叙述性回顾

介绍：顺势疗法是全球最常用的替代药物之一，在糖尿病管理方面有广泛的干预措施。 筛选糖尿病动物模型中的顺势疗法药物的作用不仅有助于验证其抗糖尿病的潜力，而且有助于了解这些药物对生命系统及其作用机制的影响。本审查的重点是收集的临床前研究的结果进行顺势疗法药物在糖尿病的管理中使用。**方法:** PubMed，HomBRex门户被搜索到11月2019。 使用的搜索词是"顺势疗法"，"糖尿病"及其网格变化。**结果:** 14项研究被列入审查。 十九种药物被评价为其抗糖尿病疗效体内或体外。 大多数的糖尿病临床前研究进行了对蒲桃和头孢桑德拉籼在母亲酊剂和效力证实其在糖尿病管理中的有效性。 除了在目前的审查中讨论的药物，还有许多其他顺势疗法药物，用于治疗糖尿病，需要科学验证全球接受的科学博爱。**结论:** 考虑到降血糖潜力、可用性和顺势疗法药物的成本效益，未来的研究应侧重于筛选其有效性的糖尿病并发症和其他代谢紊乱的管理。