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Original Article

Studies on antidiabetic herbal formulations available in the herbal stores of Karachi, Pakistan

[Estudios sobre formulaciones a base de hierbas antidiabéticas disponibles en las tiendas de hierbas de Karachi, Pakistán]

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Abstract

Context: Diabetes mellitus is a condition, which is characterized by persistent hyperglycemia, abnormal functioning of insulin and difficulty in the metabolism of carbohydrates, fats and proteins. Antidiabetic medicines of herbal origin are widely consumed in Pakistan. Therefore, there was a need to generate data on antidiabetic herbal formulations manufactured and marketed in Pakistan.

Aims: To develop a list of Pakistani manufactured antidiabetic herbal products and the most common herbal ingredients found in them.

Methods: Antidiabetic herbal formulations were collected from the renowned herbal stores of Karachi, Pakistan, and their ingredients were checked. The most common herbal ingredients found in them were determined, and the possible constituents responsible for the antidiabetic action of these herbs were discovered.

Results: A total of 15 herbal antidiabetic products were collected from the herbal stores. The most common herbs found in them include *Syzygium cumini, Gymnemma sylvestre, Aloe vera, Nigella sativa, Acacia nilotica, Commiphora myrrha, Portulaca oleracea, Punica granatum, Rhus coriaria, Coriandrum sativum, Trigonella foenum-graecum, Bambusa bambos*, *Holarrhena antidysenterica, Swertia changii, Curcuma longa* and *Rumex vesicarius.* The constituents responsible for antidiabetic activity include alkaloids, polysaccharides, glycosides, secoiridoid, phenolic acids, flavonoids, terpenoids, saponins and volatile oil.

Conclusions: The herbs incorporated in these formulations have proven antidiabetic effects; therefore, these formulations can produce significant results in the management of diabetes. More research on each of these formulations is needed to confirm the potency of all these herbal products.

Keywords: diabetes mellitus; hyperglycemia; polyherbal drugs.

Resumen

Contexto: La diabetes mellitus es una condición que se caracteriza por hiperglucemia persistente, funcionamiento anormal de la insulina y dificultad en el metabolismo de carbohidratos, grasas y proteínas. Los medicamentos antidiabéticos de origen vegetal se consumen ampliamente en Pakistán. Por lo tanto, era necesario generar datos sobre las formulaciones a base de hierbas antidiabéticas fabricadas y comercializadas en Pakistán.

Objetivos: Desarrollar una lista de productos herbales antidiabéticos fabricados en Pakistán y los ingredientes herbales más comunes que se encuentran en ellos.

Métodos: Se recolectaron formulaciones de hierbas antidiabéticas de renombradas tiendas de hierbas de Karachi, Pakistán, y se verificaron sus ingredientes. Se determinaron los ingredientes herbales más comunes que se encuentran en ellos y se determinaron los posibles constituyentes responsables de la acción antidiabética de estas hierbas.

Resultados: Se recogió un total de 15 productos antidiabéticos a base de hierbas de las tiendas de hierbas. Las hierbas más comunes que se encuentran en ellos incluyen *Syzygium cumini*, *Gymnemma sylvestre*, *Aloe vera*, *Nigella sativa*, *Acacia nilotica*, *Commiphora myrrha*, *Portulaca oleracea*, *Punica granatum*, *Rhus coriaria*, *Coriandrum sativum*, *Trigonella foenum-graecum*, *Bambusa bambos*, *Sweidia changii*, *Curcuma longa* y *Rumex vesicarius*. Los constituyentes responsables de la actividad antidiabética incluyen alcaloides, polisacáridos, glucósidos, secoiridoide, ácidos fenólicos, flavonoides, terpenoides, saponinas y aceite volátil.

Conclusiones: Las hierbas incorporadas en estas formulaciones tienen efectos antidiabéticos comprobados; por lo tanto, estas formulaciones pueden producir resultados significativos en el manejo de la diabetes. Se necesita más investigación sobre cada una de estas formulaciones para confirmar la potencia de todos estos productos a base de hierbas.

Palabras Clave: diabetes mellitus; hiperglucemia; drogas a base de plantas.

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INTRODUCTION

Diabetes mellitus (DM) is the most common endocrine disorder affecting millions of people worldwide. It is characterized by chronic hyperglycemia, hyperlipidemia, hyperaminoacedemia and decreased insulin secretion (Rao et al., 2010). There are three major types of DM: type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), and gestational diabetes. T1DM is caused by pancreatic cell death resulting in insufficient insulin secretion, leading to the demand for an exogenous supply of insulin for the patients' lifetime. On the other hand, T2DM results from insulin resistance due to the decreased sensitivity of insulin towards skeletal muscles, liver, and adipose tissues. Gestational diabetes is another type of diabetes, which occurs in women during pregnancy without any previous history of the disease (Choudhury et al., 2018).

There are various complications of diabetes such as macrovascular and microvascular complications. Macrovascular complications include cardiovascular, cerebrovascular, and peripheral vascular diseases, whereas microvascular complications include retinopathies, neuropathies, and nephropathies (Papatheodorou et al., 2016). This disease may result in a reduced quality of life and an increase in morbidity and mortality rates (Abubakar et al., 2017).

Diabetes is mainly treated with either synthetic hypoglycemic medicines or exogenous insulin. However, the usage of all of these drugs comes up with several side effects that's why the use of medicinal plants is preferred to treat diabetes mellitus and several other diseases (Moradi et al., 2018). Half of the population of developed countries depend upon complementary and alternative medicine to treat various diseases, and in developing countries, this number increases up to 75-90% (Robinson and Zhang, 2011). The natural origin of herbal drugs, easy accessibility, and relatively low side effects attract common people to use them. In Pakistan, many people prefer herbal medicines for the management of different diseases. Unani medicine is the most commonly practiced herbal system of medicine in Pakistan, whereas, in northern Pakistan, Ayurvedic medicine is also in practice (Kanwal and Sherazi, 2017). Diabetes mellitus has become very common in this region, with a prevalence of 11.77%, and the patients have consumed herbal supplements for managing its symptoms (Meo et al., 2016). Therefore, there was a need to collect information about locally manufactured herbal antidiabetic products and their common ingredients. For this reason, this study has been designed so that a data can be generated about the majority of the locally manufactured antidiabetic herbal drugs of Pakistan.

MATERIAL AND METHODS

Study area

This study was conducted in Karachi, the largest city of Pakistan and the capital of Sindh province. It is located in the southern region of Pakistan. It is a metropolitan city, and people from various ethnic groups are settled here. According to the 2017 census, the population of Karachi was estimated to be 16 051 521. Many educational institutes offering the degree of Pharmacy and Pharmacognosy are located here. A few examples are the University of Karachi, Dow University of Health Sciences, Ziauddin University, Baqai University, Hamdard University, Jinnah Sindh Medical University, Nazeer Hussain University, Salim Habib University, Jinnah University for Women, Benazir Bhutto Shaheed University Lyari, Iqra University, and Shaheed Benazir Bhutto Dewan University. Some well-recognized universities such as Hamdard University and Ziauddin University are also running a 5-year Bachelor of Eastern Medicine (B.E.M.S) program in Karachi, Pakistan, where students are also completing postgraduate studies in this discipline.

Survey of herbal stores and herbal practitioners

The survey mainly consisted of face-to-face interviews with herbal practitioners and herbal storekeepers. The survey was conducted in the southern city of Pakistan (Karachi, State: Sindh). Since this city is quite large and densely populated, the Central, South, East, and Malir districts of Karachi were selected to perform this survey (Figs. 1-2). The survey was conducted in two phases, in which the first phase lasted from 20 January 2020 to 28 July 2020, and the second phase lasted from 1 June 2021 to 31 August 2021. Herbal practitioners who were graduates of recognized universities and herbal storekeepers of well-recognized herbal stores were included in this study. A total of 25 herbal practitioners and 10 herbal storekeepers had participated in this survey. The interviews were mainly conducted in the Urdu language. Data was generated about the locally manufactured antidiabetic herbal medicines. Only those medicines were selected, which were manufactured by renowned herbal laboratories. The unauthentic herbal preparations, in

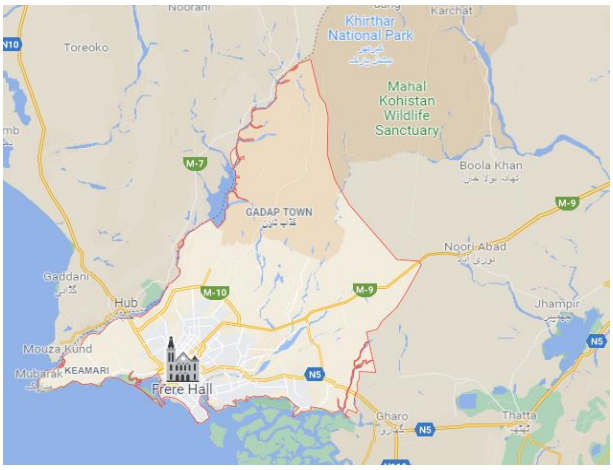

Figure 1. Map of Karachi city.

(Photo source: Google maps).

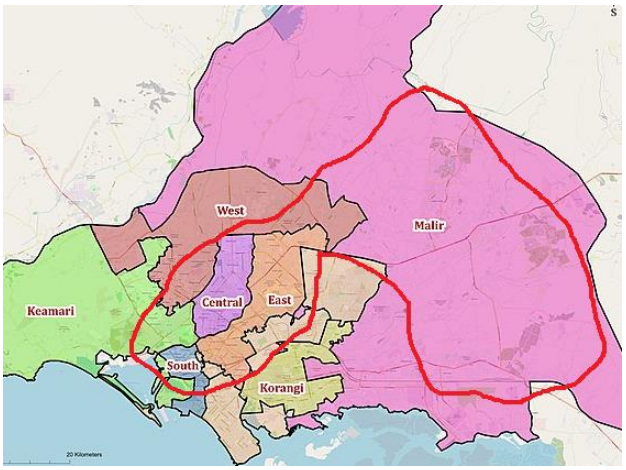

Figure 2. Map of the area covered in this survey-based study (red line indicating the area covered in this survey).

(Photo source: Wikipedia.org).

Table 1. Characteristics of herbal practitioners.

Variable	Specification	Percentage (%)
Age	25-30	20
	30-40	80
Sex	Male	68
	Female	32
Level of education	Bachelors	76
	Postgraduate (M. Phil & Ph. D)	24
Method of treatment	Herbal	100

which the names of ingredients were not clearly mentioned were excluded. A total number of 15 herbal medicines were included. The drugs were either in solid dosage form (tablets, capsules and powders) or in liquid dosage form (oil for oral use). All the ingredients found in them were determined. Furthermore, the literature was surveyed from Google Scholar, PubMed, and Scopus, in which the antidiabetic activities of the most common herbs found in these herbal formulations were searched in order to determine the effectiveness of these drugs.

Statistical analysis

The statistical analysis was performed by using descriptive analysis. Since numerous herbs were incorporated in each formulation, only those present in more than one formulation are considered for further research.

RESULTS

Identity of respondents

A number of 35 individuals have responded to the interview. Among them, 25 were herbal practitioners and 10 were herbal storekeepers. The characteristics of herbal practitioners are stated in Table 1, and the details of herbal storekeepers are mentioned in Table 2.

Table 2. Characteristics of herbal storekeepers.

Variable	Specification	Percentage (%)
Age	25-35	50
	35-40	50
Sex	Male	100
Level of education	Intermediate	20
	Matriculation	50
	Middle Pass	30

Table 3. The dosage form and ingredients found in anti-diabetic herbal formulation.

No.	Name of herbal product	Type of formulation	Manufacturer name	Name of ingredients
1	Ziabee	Solid (tablets)	Tayyebi Dawakhana	*Gymnema sylvestre, Syzygium cumini, Tamarindus indica, Elletaria cardamomum,* Asphaltum, Tin Calx, Iron Calx, Emerald Calx
2	Habbe Khas	Solid (tablets)	Tayyebi Dawakhana	*Crocus sativus, Physter microcephalus, Myrictica fragrans, Alpinia glance, Delphinum denudatum, Garcinia morella*, Iron calx, *Nux vomica,* Silver foil
3	Dawa-i-Ajeeb Ziabetis	Solid (tablets)	Ajmal DawaKhana	*Portulaca oleracea, Syzygium cumini, Punica granatum, Rhus coriaria*, *Lactuca sativa, Rosa indica, Gallus domesticus, Coriandrum sativum,* Iron, Emerald, *Oinctada margeritifera*
4	Diabet Powder	Solid (powder)	Farzana Dawakhana	*Syzygium cumini, Nigella sativa*, *Aloe vera, Commiphora myrrha.*
5	Diabet off Tablets	Solid (tablets)	Farzana Dawakhana	*Syzygium cumini, Nigella sativa*, *Commiphora myrrha.*, *Aloe vera, Medicago sativa*
6	Zubex	Solid (tablets)	Qarshi Industries Pvt. Ltd.	*Curcuma longa, Syzygium cumini* seeds, Iron Murakkab, Egg shell Calcium (processed), Asphaltum
7	Hemani Black seed oil	Liquid (oil)	Hemani Herbals	*Nigella sativa.*
8	Diabeguard Capsules	Solid (capsules)	Meyar Herbal Laboratories	*Gymnema sylvestre, Trigonella foenum-graecum, Syzygium cumini, Momordica charantia*
9	Qurs Ziabetus	Solid (tablets)	Hamdard Laboratories Waqf Pakistan.	*Santalum album, Bambusa bambos, Rumex vesicarius, Punica granatum, Portulaca oleracea, Lactuca scariola, Rhus coraria* (dried), *Coriandrum sativum, Armenian bole* (flowers), *Acacia nilotica* (gum), *Maranta arundinaceae (*paste), Gelatin paste, Camphor, Rectified spirit, Liquid paraffin, Soapstone, Magnesium carbonate
10	Dolabi Tablets	Solid (tablets)	Hamdard Laboratories Waqf Pakistan.	*Acacia nilotica*, *Bambusa bambos*, *Rumex vesicarius, Gymnema sylvestre*, *Syzygium cumini*, Gond safaid, labba buz, kushta baize murgh, Khushta khabsul hadeed, Kushta jast
11	Garlina	Solid (tablets)	Hamdard Laboratories Waqf Pakistan.	*Allium sativum, Allium cepa, Zingiber officinale, Nigella sativa, Commiphora mukul.*
12	Sufuf Khasta Jamun	Solid (powder)	Hamdard Laboratories Waqf Pakistan	*Syzygium cumini, Gymnema sylvestre*, *Momordica charantia, Holarrhena antidysenterica, Swertia changii, Terminalia bellirica*
13	Ziabeen	Solid (tablets)	Ashraf Laboratories Pvt. Ltd.	*Aloe barbadensis, Azadirachta indica, Syzygium cumini, Gymnema sylvestre, Momordica charantia, Holarrhena antidysenterica, Swertia changii, Piper nigrum*, *Acacia senegal* (gum).
14	Methi Capsules	Solid (capsules)	Bakhshi Dawakhana	*Trigonella foenum-graecum.*
15	Antidiabetic Herbal Capsules	Solid (capsules)	Rehan Herbal Laboratories	*Prunus avium, Cinnamomum zeylanicum* (bark), *Curcuma longa, Lawsonia inermis, Swertia changii, Patinaca sativa, Artemisia absinthium, Caesalpinia bonducella, Citrullus colocynthis.*

Ingredients found in the antidiabetic herbal products

The dosage form and the ingredients found in the herbal formulations are listed in Table 3.

Common ingredients found in the herbal products

The most common herbal ingredients found in these herbal preparations are mentioned in Table 4.

Possible active principles of herbs responsible for antidiabetic effects

Literature was surveyed to find out the chemical constituents responsible for the antidiabetic activity of these herbs, which are mentioned in Table 5.

DISCUSSION

The present study reveals that a vast majority of herbs are incorporated in these herbal antidiabetic

Table 4. List of most common ingredients found in these formulations

No.	Family	Name of Ingredients	Frequency	Percentage (%)
1	*Myrtaceae*	*Syzygium cumini* (L.) Skeels	8	53.33
2	*Apocynaceae*	*Gymnema sylvestre* (Retz.) R.Br. ex Sm.	5	33.33
3	*Ranunculaceae*	*Nigella sativa* L.	4	26.66
4	*Asphodelaceae*	*Aloe vera* (L.) Burm.f.	3	20.00
5	*Leguminosae*	*Acacia nilotica* (L.) Delile	3	20.00
6	*Burseraceae*	*Commiphora myrrha* (Nees) Engl.	2	13.33
7	*Portulacaceae*	*Portulaca oleracea* L.	2	13.33
8	*Lythraceae*	*Punica granatum* L.	2	13.33
9	*Anacardiaceae*	*Rhus coriaria* L.	2	13.33
10	*Umbelliferae*	*Coriandrum sativum* L.	2	13.33
11	*Leguminosae*	*Trigonella foenum-graecum* L.	2	13.33
12	*Poaceae*	*Bambus bambos* (L.) Voss.	2	13.33
13	*Apocynaceae*	*Holarrhena antidysenterica* (Roth) Wall ex A.DC.	2	13.33
14	*Gentianaceae*	*Swertia changii* S.Z. Yang, C.-fan Chen & Chih H.Chen	2	13.33
15	*Zingiberaceae*	*Curcuma longa* L.	2	13.33
16	*Polygonaceae*	*Rumex vesicarius* L.	2	13.33

Table 5. List of the active principles responsible for antidiabetic effects of these formulations.

No.	Ingredient names	Active ingredient names
1	*Syzygium cumini* (L.) Skeels	Alkaloid (jambosine), glycoside (jambolin) and mycaminose (Ayyanar and Subhash-Babu, 2012; Kumar et al., 2008)
2	*Gymnema sylvestre* (Retz.) R.Br. ex Sm.	Gymnemic acid (Kanetkar et al., 2007)
3	*Nigella sativa* L.	Thymoquinone, volatile oil of *N. sativa* (Bamosa, 2015)
4	*Aloe vera* (L.) Burm.f.	Glucomannan polysaccharides (Yagi et al., 2009)
5	*Acacia nilotica* (L.) Delile	Heteropolysaccharide or high molecular weight polysaccharides (Sharma, 1985)
6	*Commiphora myrrha* (Nees) Engl.	Furanosesquiterpenes (Al-Romaiyan et al., 2020)
7	*Portulaca oleracea* L.	Poly-unsaturated fatty acids, glutathione, flavonoids, polysaccharides, glutathione, antioxidants and vitamins (El-Sayyed, 2011)
8	*Punica granatum* L.	Oleanolic acid, ursolic acid and gallic acids (Katz et al., 2007)
9	*Rhus coriaria* L.	Gallic acid, methyl gallate, kaempferol and quercetin (Shidfar et al., 2014)
10	*Coriandrum sativum* L.	Polyphenolics and volatile components (Asgarpanah and Kazemivash, 2012)
11	*Trigonella foenum-graecum* L.	Dietary fiber, saponins, 4-hydroxyisoleucine and pectin (Gupta et al., 2001)
12	*Bambus bambos* (L.) Voss.	β-sitosterol glycoside and stigmasterol (Nazreen et al., 2011)
13	*Holarrhena antidysenterica* (Roth) Wall ex A.DC.	Steroidal alkaloids, flavonoids, triterpenoids, phenolic acids, tannin, resin, coumarins, saponins and ergostenol (Sinha et al., 2013)
14	*Swertia changii* S.Z. Yang, C.-fan Chen & Chih H.Chen	Magniferin, swertiamarin and amarogentin (Phoboo et al., 2010)
15	*Curcuma longa* L.	Curcumin, demethoxycurcumin, bisdemethoxycurcumin and ar-turmerone (Kuroda et al., 2005)
16	*Rumex vesicarius* L.	More research is needed to identify the constituents responsible for antidiabetic activity of this plant.

medicines. Among them, *Syzygium cumini* is the most commonly utilized herb in these formulations. The antidiabetic effect of *Syzygium cumini* was also confirmed by various research such as a study conducted by Kumar et al. (2008) revealed that the ethyl acetate and methanolic extracts of the *Syzygium cumini* seed powder have potential antidiabetic effect at the dose of 200 and 400 mg/kg. Similarly, another commonly utilized herb *Gymnemma sylvestre* showed proven antidiabetic effects as Kanetkar et al. (2007) described that the gymnemic acid present in this species competes with glucose absorption in the intestine, thereby inhibiting glucose absorption in this site, which eventually leads to hypoglycemic effects.

Nigella sativa is the other commonly utilized herb in these polyherbal formulations. Its antidiabetic activity is confirmed by research conducted by Ahmad et al. (2009), in which *Nigella sativa* oil was administered to the diabetic subjects, and it significantly decreased fasting blood sugar compared to the control.

Another herb incorporated in these formulations, namely *Commiphora myrrha* can inhibit α-amylase, glucosidase, and acarbose activities in a concentration-dependent manner (Abdel-Hady et al., 2019).

Portulaca oleracea also decreases fasting blood glucose levels and increases fasting serum insulin levels and insulin sensitivity index (Bai et al., 2016).

Punica granatum flower and juice may slow down the prognosis of diabetes by binding with PPAR-γ receptors and producing nitric oxides. Ursolic acid, gallic acids and oleanolic acids are the components responsible for the antidiabetic effects of *Punica granatum* (Katz et al., 2007).

The ethanolic extract of the fruits of *Rhus coriaria* has the potential to control postprandial hyperglycemia, probably by inhibiting α-glucosidase from declining the digestion or absorption of carbohydrates. Furthermore, it also produces antioxidant activity by increasing the levels of superoxide dismutase and catalase enzymes of the red blood cells. This clearly indicates that *Rhus coriaria* can prevent the long-term complications of diabetes (Mohammadi et al., 2010).

The leaves and stem of *Coriandrum sativum* could produce hypoglycemic effects, and they can produce antidiabetic effects by restoring the beta cells of the pancreas and improving the effects of insulin on blood sugar. The phenolic constituents present in *Coriandrum sativum* could be responsible for these effects (Sreelatha and Inbavalli, 2012).

The seeds of *Trigonella foenum-graecum* may also enhance insulin sensitivity and reduce insulin resistance in type 2 diabetic patients. The dietary fiber present in *Trigonella foenum-graecum* may contribute to its antidiabetic potential. Due to the presence of pectin, the seeds of *Trigonella foenum-graecum* may prolong gastric emptying time and thus decrease the absorption of carbohydrates in the blood. An amino acid present in *Trigonella foenum-graecum,* namely 4-hydroxyisoleucin may produce antidiabetic effects by increasing insulin secretion from the pancreas's beta cells (Gupta et al., 2001).

Bambusa bambos can reduce blood sugar levels, increase the levels of antioxidant enzymes such as SOD and CAT, decrease lipid peroxidation and normalize the GSH levels in the pancreas of diabetic rats (Nazreen et al., 2011).

The seeds of *Holarrhena antidysenterica* may reduce blood glucose levels, possibly by acting as an insulinotropic agent. Furthermore, it may also alter the condition of diabetes-induced hyperlipidemia (Ali et al., 2009).

According to research conducted by Phoboo et al. (2013), it was found that the different parts of the plant *Swertia changii* showed potential antioxidant activity, and its aqueous and ethanolic extracts also showed α-glucosidase inhibiting activity.

Another study found that the rhizomes of *Curcuma longa* may produce antidiabetic activity via activating PPAR-γ (Kuroda et al., 2005).

Another plant found in some of these herbal medicines, namely *Rumex vesicarius*, decreased blood sugar levels in streptozotocin-induced diabetic rats at different doses and protected pancreatic cells from streptozotocin induced-damages. The research concluded that the ethanolic extract of *Rumex vesicarius* might produce antidiabetic effects by increasing insulin secretion by the pancreas (Reddy et al., 2016).

CONCLUSION

The herbal products marketed in the herbal stores of Karachi, Pakistan, for diabetes treatment may have the ability to manage the symptoms and complications of this disease since the herbs incorporated in them possess proven antidiabetic effects. These formulations consist of numerous herbs that produce antidiabetic effects following multiple mechanisms, and a variety of active constituents may be responsible for the antidiabetic activity. Extensive research on the efficacy and toxicity of these herbal formulations is recommended to analyze their therapeutic and hazardous effects on human subjects.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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AUTHOR CONTRIBUTION:

Contribution	Shah E
Concepts or ideas	x
Design	x
Definition of intellectual content	x
Literature search	x
Experimental studies	x
Data acquisition	x
Data analysis	x
Statistical analysis	x
Manuscript preparation	x
Manuscript editing	x
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