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Introduction

Prevalence and History of Diabetes

There has been a pronounced upsurge in worldwide diabetes prevalence during the past few decades, more notably in developing countries, owing to the rapid globalisation and changing lifestyles. Diabetes-associated complications, such as coronary artery and peripheral vascular disease, stroke, diabetic neuropathy, amputations, renal failure, and blindness, also add to this burden. According to the recent IDF estimates, 1 in 11 adults is affected by diabetes. Diabetes-related deaths (5 million) were also higher than the total number of deaths caused by HIV (1.5 million), tuberculosis (1.5 million), and malaria (0.6 million) combined. Nearly 415 million people worldwide are estimated to have diabetes, and IDF has raised the concern that by 2040 almost 642 million people, or 1 adult in 10, will have diabetes [1, 2].

History of diabetes dates back to 3500 years ago where the first ever mentioning of clinical features similar to diabetes mellitus is found to have been made in greatest Egyptian medical document *Ebers Papyrus* in 1500 BC (Ebbell 1937). Descriptions of this devastating disease have also been found in ancient Indian and Chinese medical literature, as well as in the work of ancient Greek and Arab physicians [3]. Indian physicians named the condition 'madhumeha' or 'honey urine' observing that the urine from diabetes-affected individuals attracted ants and flies [4]. Apollonius of Memphis is believed to have coined the term 'diabetes' in 230 BC, meaning 'to pass through', and it was Aretaeus of Cappadocia (second century AD) who provided the first accurate description of diabetes [5]. Later on the Indian physicians, Sushruta and the surgeon Charaka (400–500 AD) differentiated

between the two types of diabetes primarily based on their occurrence in lean or overweight individuals [5, 6].

Remarkable advancements in understanding and management of diabetes took place in the nineteenth century, mostly attributable to the significant progress achieved in various scientific disciplines. Until the discovery of insulin in the 1920s by Banting and colleagues, diabetes treatments mostly adapted highly crude methods for which the success rates were extremely poor [5], and physicians of those times used to make interesting recommendations such as 'oil of roses, dates, raw quinces and gruel, jelly of viper's flesh, broken red coral, sweet almonds, and fresh flowers of blind nettles' which represented a variety of beliefs and practices of the times [7]. There are also mentions of opium being prescribed liberally [7, 8] (probably for easing the symptoms of complications like gangrene). Of note, in 1897, the average life expectancy for a 10-year-old child diagnosed with diabetes was 1.3 years, compared with 4.1 years for a 30 years old [9].

The first ever scientific remedy, discovered in 1922, and awarded with the Nobel Prize in 1923, insulin turned out to be a major advancement in treating diabetes and enabled patients to live near normal life [3, 10]. The first ever oral scientific remedy sulphonylurea was added to the treatment armamentarium, only in the 1950s. Consequently, other oral scientific remedies with diverse mechanisms of action such as metformin, glucosidase inhibitors, and insulin sensitizers were discovered, enabling better management of the disease. Currently, our treatment armamentarium consists of a vast array of technologies and therapeutic options to make individualised treatment more of a reality. Depending on the type of diabetes and its aetiology, patients may be treated with oral drugs or injectables or sometimes, a combination of both. For absolutely insulin-deficient T1DM patients, insulin pump therapy or multiple daily insulin injections are the only scientifically recognised modalities of therapy in the absence of which, subjects are likely to die. With such advances in modern medicine, a dramatic improvement in life expectancy has been noted

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after 1940. As per WHO, the average lifespan of a child born in 2015 is predicted to be 71.4 years, whereas earlier estimates of global life expectancy were 30.9 years in 1900, 46.7 in 1940, and 61.13 in 1980 [11, 12].

Complementary and Alternative Medicine

Definition and Epidemiology

According to National Center for Complementary and Integrative Health (NCCIH), a subsidiary of the National Institutes of Health (NIH), USA, Complementary and Alternative Medicine (CAM) are those healthcare approaches that have developed outside the realm of conventional medicine. Types of complementary and alternative health approaches fall into one of the two subgroups, viz. natural products or mind and body practices. Natural products (available widely and often sold as dietary supplements) consist of herbs (or botanicals), vitamins and minerals, and probiotics. Mind and body practices include a variety of procedures or techniques administered or taught by a trained practitioner or teacher (e.g. yoga, chiropractic and osteopathic manipulation, meditation, massage therapy, acupuncture, relaxation techniques, tai chi, etc.). However, some approaches may not neatly fit into either of these groups, e.g. the practices of traditional healers, Ayurvedic medicine, traditional Chinese medicine, homoeopathy, and naturopathy [13].

Of the various demographic descriptors and characteristics of users documented for an inclination towards CAM, more consistent ones include being female, more highly educated, wealthier, employed, and having private health insurance [14–17]. Research has also demonstrated that individuals who possess positive health behaviours and exhibit fewer health risk factors are more frequent CAM users [18].

According to the statistics from 2012 National Health Interview Survey (NHIS), 33.2% of US adults and 11.6% of US children aged 4 to 17 used complementary health approaches. The most commonly used approach was natural products (dietary supplements other than vitamins and minerals). Of the mind and body approaches, most commonly used by adults included yoga, chiropractic or osteopathic manipulation, meditation, and massage therapy. The popularity of such practices might definitely increase in coming years as evident from the data on the percentage of adults who practise yoga. Percentage of followers of this system of practice was found to be increased substantially, from 5.1% in 2002 to 6.1% in 2007 and 9.5% in 2012. As per the survey, nearly 59 million Americans spend money out-of-pocket on complementary health approaches, and their annual spending totalled around 30 billion dollars [19, 20].

Possible Reasons Towards CAM Popularity

A vast majority of patients opt for CAM therapies as a complement to conventional care rather than as an alternative choice [21]. In a US-based study, total visits to complementary medical practitioners (629 million) exceeded total visits to US primary care physicians (386 million) [22]. Traditional CAM practices are extremely popular in South-Asian countries, where modern conventional medicines are often inaccessible and unaffordable to the majority of the individuals. Therefore despite the perception about the efficacy of modern medicines, traditional medicine continues to relish acceptance among these populations [23].

Several factors have been noted as reasons for the extensive use of these rather scientifically unproven methods of CAM therapies (Table 64.1). Dissatisfaction arising from conventional therapies, at times, clubbed with higher treatment expenses, concern over side effects of drugs, an urge to have a grip on the course of the disease, and a notion of CAM therapies being compatible with patient's values and beliefs [17, 24–27], are some of them. Patient's expectations of their efficacy [27, 28], advanced stage of the disease [29, 30], experiences with conventional healthcare professionals and complementary medicine practitioners, and 'healthcare pluralism' are also identified as the reasons for this widespread acceptability of CAM therapies. The latter term describes the fact that when people become ill, they can opt for seeking assistance and treatment advice from diverse sources ranging from friends/ family, conventional/CAM practitioner, etc. which essentially will have an impact on their treatment choices [31, 32]. Analysis of 2002 National Health Interview Survey pointed out that around 6 million American adults had opted CAM therapies predominantly because they found conventional medical treatments unaffordable. Among 63% of the individuals who faced such cost constraints, herbal remedies were found to be the most popular approach [33].

Table 64.1 Reasons for CAM popularity

Belief that CAM practices are devoid of any side effects and are totally safe
Noninvasive nature
Easy accessibility
Advanced stage of the disease and unpleasant experiences with conventional healthcare professionals
As recommended by someone close (family members, friends, etc.)
Pleasant therapeutic experience
Modern conventional medicines being inaccessible and unaffordable
Dissatisfaction arising from conventional therapies
Poor doctor/patient relationship
Insufficient time with doctor
Concern over side effects of drugs
An urge to have a grip on the course of disease
Notion of CAM therapies being compatible with patient's values and beliefs

CAM Therapies for Diabetes Management

Many Antidiabetic Medications Have a Natural Origin

Many of the standard conventional drugs have a history of natural origin. However, administering them in their natural form may not be of much benefit. Phytochemicals or compounds present in the natural sources often serve as 'lead' newer analogues could be derived from some of them. This search for novel bioactive from nature – plants, animals, or microflora – still continues to widen our treatment armamentarium. Estimates suggest that around one-half of all licenced drugs that were registered worldwide in the 25-year period prior to 2007 were either natural products or their synthetic derivatives [34, 35].

Over 400 traditional plant treatments for diabetes have been reported, and only a few of them have undergone valid scientific scrutiny to prove their safety and efficacy [36]. Metformin, a popular antidiabetic drug and widely accepted first-line agent, was derived from a traditional antidiabetic plant *Galega officinalis* (goat's rue or French lilac) [37] whose active ingredient was found to be glargine or isoamylene guanidine. While guanidine and certain derivatives were found to have toxic effects, the biguanides (two linked guanidine rings) turned out beneficial and were available for therapeutic use since the 1950s [38]. Further research confirmed the antihyperglycaemic efficacy of metformin without causing overt hypoglycaemia or weight gain. Metformin in addition to its antihyperglycaemic properties also stands out for its effects beyond glycaemic control such as improvements in endothelial dysfunction, haemostasis and oxidative stress, insulin resistance, lipid profiles, and fat redistribution [39, 40]. The UK Prospective Diabetes Study demonstrated that early use of metformin reduced cardiovascular mortality and increased survival in overweight and obese T2DM patients beyond that expected for the prevailing level of glycaemic control [41]. This proven efficacy, safety, beneficial cardiovascular and metabolic effects, and its capacity to be associated with other antidiabetic agents make metformin the first line of choice for T2DM patients [42] and is included in the World Health Organization (WHO) list of essential medicines [43]. Phlorizin, isolated from the bark of apple trees, was found to cause glycosuria [44] but later led to the discovery of better analogues with SGLT2-inhibiting activity such as dapagliflozin, empagliflozin, and canagliflozin [45, 46].

Likewise, exenatide and highly accepted insulin with antidiabetic activities have their origin from animals. The discovery of insulin by Frederick Banting and Charles Best in 1921 was indeed a major breakthrough in the treatment of diabetes, and it all began with a murky concoction of

canine pancreas extract [34, 47]. Exenatide, a glucagon-like peptide-1 (GLP-1) agonist is a synthetic version of exendin-4, a hormone found in the venom of Gila monster *Heloderma suspectum* which was isolated by Dr John Eng in 1992 [48, 49]. This drug has been approved for use in T2DM management [50].

Apart from antidiabetic compounds of plant and animal origin, some have been derived from microbes. Examples include acarbose (from *Actinoplanes* sp.), miglitol (from *Bacillus* and *Streptomyces* sp.), voglibose (from *Streptomyces hygroscopicus* subsp. *limoneus*) [46], etc. The alpha-glucosidase inhibitor acarbose used in T2DM is a pseudo-oligosaccharide isolated from the culture broths of various actinomycetes [51]. It is probably the most widely used digestive enzyme inhibitor for the treatment of T2DM, acting on α -glucosidase, α -amylase, sucrase, and maltase but without insulinotropic properties [52]. With regulated research and controlled clinical trials, there is a higher probability that many more natural agents could be incorporated into the modern stream of medicine.

Prevalence and Patterns of CAM Use Among Diabetes Patients

According to Villa-Caballero and colleagues, the presence of diabetes is a predictor of CAM use, and ethnicity determines the types of CAM followed. Of the different CAM modalities, biologically based practices (e.g. dietary supplements, herbal products, and botanical products) are the most commonly used and studied for treating diabetes [53, 54] which is probably due to their wider and cheaper availability and also being inherent in the cultures and ancestral beliefs of the individuals. Egede et.al using the data from 1996 Medical Expenditure Panel Survey compared the prevalence and pattern of use of complementary and alternative medicine (CAM) in individuals with and without diabetes and identified factors associated with CAM use. Analysis revealed that diabetes-affected individuals were 1.6 times more likely to use CAM than those without diabetes, and the most commonly used CAM therapies among diabetes patients were found to be, in the order of importance, nutritional advice and lifestyle diets, spiritual healing, herbal remedies, massage therapy, and meditation training [55]. Another study from Israel reported that almost every fourth patient with diabetes uses CAM [56]. India, a country with a rich history of traditions, rituals, and healing practices, has a very high CAM use of 67% among its diabetic population of which majority (97%) used naturopathy, which often included herbalism [57]. An ethnographic research conducted in Kerala revealed that the patient's perceptions of disease as well as its management are influenced by their cultural background and environmental resources. Many of them

frequently used Ayurvedic and traditional herbal medicines as supplements to conventional therapy [58].

The National Center for Complementary and Alternative Medicine (NCCAM now renamed as NCCIH) conducted an analysis of the data from the National Center for Health Statistics, Centers for Disease Control and Prevention (CDC), and demonstrated that, among adults with T2DM, 30.9% used complementary medicine for any reason, but only 3.4% used complementary medicine to treat or manage their T2DM versus 7.1% of those with T1DM. Almost 77% of the T2DM patients, who used complementary medicine to treat/manage their disease, used it in conjunction with their conventional prescription medicine. Furthermore, individuals with more severe diabetes were predicted to be more likely to use complementary medicine. The most prevalent types of complementary medicine therapies followed included diet-based interventions and non-vitamin/non-mineral dietary supplements [30]. In a study that determined the nature and prevalence of dietary supplement use among chronically ill children, 60% of the patients with T1DM reported using supplements to manage their disease and 31% admitted non-prescribed use [59].

Concerns with CAM Therapies

Widespread use of CAM practices poses several risk factors (see Table 64.2) such as the patients getting overloaded with consecutive unsuccessful therapeutic measures owing to false diagnosis, running into life-threatening situations, adverse effects, and hidden costs of treatment. Opting for these unconventional practices might delay the initiation of effective mod-

Table 64.2 General concerns associated with CAM therapies

Adverse drug interactions
Patient's belief of receiving optimum therapy and finally running into life-threatening conditions and increased treatment costs
CAM products not meeting quality standards due to reasons such as:
Products being adulterated with conventional medicines to achieve/enhance the efficacy
Inadvertent incorporation of unintended constituents due to errors with herb selection, good manufacturing procedures, etc.
Intra and inter-product variations
Mislabelling of the contents
Poor quality of the clinical trials making it difficult to arrive at a definite conclusion regarding efficacy and safety of CAM practices
Patient's prejudice that CAM therapies are natural and safe, which increases their tendency towards self-treatment practices and use of over-the-counter products
Lack of proper communication between the patients and health practitioners regarding CAM use
Polypharmacy with CAM and conventional treatments resulting in decreased medication adherence and more negative quality of life
Lack of stringent regulations to guard against quackery in CAM practices

ern conventional treatments and thereby increase the chances of treatment failures and unbearable treatment expenses [60–64]. Drug-herb interactions, which compromise the quality of products due to adulteration or presence of inappropriate amounts of active ingredients, lack of proper regulations on various CAM practices and CAM practitioners, underdeveloped research, poor quality of clinical trials, false claims and fake publicity, absence of proper communication with health practitioners, etc., are all known to be contributing risk factors towards the failure of CAM therapies [65–68].

Compromised Quality of CAM Products

Lack of proper adherence to manufacturing, marketing, and storage protocols might lead to deterioration in product quality, viz. contamination with undesirable substances, intra-product and inter-product variations, mislabelling of the contents, misidentification, etc., which leaves us highly unsure regarding their safety and efficacy [61, 69–71]. Considering the example of herbs, they do not have a consistent, standardised composition, and different plant parts have a different profile of constituents. Furthermore, several factors such as climate, growing conditions, time of harvesting, and post-harvesting issues such as storage conditions and processing are all known to influence the content and concentration of constituents. Although standardisation of many of these products has been implemented, it may not be always feasible since active constituents of many botanicals are still unknown [31]. In a meta-analysis conducted, high variability in ginsenoside levels in ginseng across different source parameters, viz. ginseng type, assay technique, and ginsenoside type, was shown to result in high variability in their efficacy. This is a warning signal that the reported safety and efficacy data of a particular product may highly differ when compared to other over-the-counter batches, preparations, varieties, and species of the herb [72].

Many US-manufactured and Indian-manufactured Ayurvedic medicines that were sold over the Internet were adulterated with unacceptable levels of lead, mercury, or arsenic [73], and serious consequences were also reported with the use of 'herbal' products that contained 'hidden' active drug compounds or heavy metal contaminants [74–78]. Centers for Disease Control and Prevention (CDC), USA, had reported lead intoxication from Ayurvedic medications among pregnant women [79]. Since 2007, the FDA has imposed an import alert on certain Ayurvedic products to prevent such products from entering the United States [80]. Accidental or intentional contamination of CAM products with conventional drugs (e.g. corticosteroids) or poisonous substances (e.g. heavy metals, pesticide residues) and microorganisms are also reported [81, 82]. Chinese 'herbal' creams were found to contain corticosteroids [83], and some

Indian Ayurvedic remedies contained heavy metals [74]. Likewise, deterioration in the quality of 'homoeopathic' remedies [84, 85] as well as that of therapeutic essential oils [86] is also a major concern. Another classic example is 'Chinese herb nephropathy', where weight-reduction pills supposed to contain the herb *Stephania tetrandra* were inadvertently contaminated with nephrotoxic herb *Aristolochia fangchi*, causing nephropathy and/or cancer in women attending a slimming clinic in Belgium [87–89].

Complications from Drug Interactions

When CAM products such as herbal medicines or dietary supplements are used concomitantly with conventional drugs, a very common practice, there may be a potential for drug-product interactions. Product-product interactions may also occur when many of these products are used concurrently [90]. These interactions often alter the pharmacokinetics or pharmacodynamics of conventional drugs, thereby altering their absorption, distribution, metabolism, and/or excretion [66, 67]. Herbs possessing hypoglycaemic activity like ginseng, garlic, and bitter melon are all reported to have additive effects in patients taking oral hypoglycaemics or insulin [72, 91–93]. In contrast, dietary gums (e.g. gum guar) usually prescribed to overcome postprandial hyperglycaemia were found to reduce the absorption of hypoglycaemic agents like metformin and glibenclamide by prolonging gastric retention [92, 94, 95]. Since diabetes patients are often burdened with many other comorbidities, the majority of them would require lifelong polypharmacotherapy (multiple medications) and hence stands at increased risk of such harmful drug interactions [96].

Underdeveloped Research and Poor Quality of Clinical Trials

Unlike conventional medicine, CAM in general lacks an established research infrastructure, and therefore many of the already available scientific evidence are methodologically weak, or outright flawed [97–101]. Measures such as the implementation of CONSORT guidelines [102, 103] for reporting and the establishment of a 'field' for CAM in Cochrane database [104] have allowed us to make a more reliable assessment of the safety and efficacy of these systems of medicinal practices [101].

False Claims and Fake Publicity

Alternative medicine is widely promoted among the public, and some of them even claim these therapies to be highly

effective with no side effects [105]. The inherent notion among the public that these therapies are 'natural' and hence 'completely safe' enables easier exploitation by advertisers and commerce. The absence of stringent regulations in many countries can allow exaggerated claims to be made, and this is more pronounced in areas of commerce that are difficult to control, for example, products sold over the Internet [106]. It is often seen that the lay literature and even certain 'professional' texts based on some CAM practices make unsubstantiated medical claims as well as encourage self-treatment for even some serious conditions [31, 107]. In India, 'The Drugs and Magic Remedies (Objectionable Advertisements) Act', 1954, controls the advertising of drugs and restricts advertisements of such 'wonder drugs or remedies' [108].

Lack of Proper Regulations and Policies

Among WHO's 191 countries, only 25 have a national policy on TM/CAM, and only 64 countries regulate herbal medicines [109]. The WHO has published a series of technical guidelines and reviewed regulations on herbal medicines in the document *Regulatory Situation of Herbal Medicines: A Worldwide Review* [110]. In the United States, national non-governmental organisations, such as the Accreditation Commission for Acupuncture and Oriental Medicine, the American Board of Medical Acupuncture, the Council of Chiropractic Education, etc., accredit education in some of them, while most other nations are devoid of these [68]. In the United States prior to 1994, CAM supplements were classified as either foods or drugs depending on the intended use, and later Dietary Supplement Health and Education Act (DSHEA 1994) framed a better definition for 'dietary supplement'. It effectively took out any product containing a vitamin, mineral, herb, or amino acid marketed as a supplement to the normal diet, from obtaining USFDA approval. This legislation allows such products to forego the stringent approval processes and does not require any proof of their safety and efficacy before being marketed. However, this has led to the situation where many of them are available over-the-counter even in grocery stores [61, 111].

Similar is the situation of CAM practitioners in many countries where they are not regulated in any manner. There are no systems in place to evaluate the training or expertise of these practitioners [68, 112–114]. In rural areas where timely access to treatment is challenging, this poses a major problem. Many of the times, local practitioners become the primary point of approach, and thus the lack of authentic therapists can aggravate the situation [68, 114]. Therefore, imposing restrictions on CAM practitioners without any acceptable educational qualifications and adopting standards of practice should be given due priority to minimise such practice risks [115].

Absence of Proper Communication with Health Practitioners

When the extent of patients' utilisation of complementary medicine and their knowledge and attitude regarding the same were studied by Giveon et al., more than half of the respondents believed that natural drugs are safe with no side effects. Users may not relate their symptoms to CAM and not disclose its use to their physician, leading to complications such as delayed diagnosis and treatment, delaying or replacing a more effective form of treatment or even compromise the efficacy of certain conventional drugs. The situation becomes even worse when CAM users are advised by the healers to discontinue the use of prescription drugs, particularly in those with chronic disease conditions [116]. CAM practitioners usually do not encourage inquiries regarding the constituents of their preparations, and most patients are least interested to know about the same as they consider such preparations to be 'natural' otherwise, 'safe'. Healthcare professionals are mostly unaware of CAM use by their patients and are not consulted prior to their use [117]. Unfortunately, there are also instances where, even when the physicians are aware of their patients using such unproven remedies, they may not be trained to recognise potentially serious side effects [33]. Therefore, it becomes practically impossible to apprehend whether CAM therapy played any significant contributory role towards the efficacy or failure of conventional treatment [118].

In its Position Statement on 'Unproven Therapies', ADA raises the concern that most patients do not disclose the use of alternative medicine, and hence conventional practitioners need to specifically ask their patients about the same. ADA continuously evaluates the usefulness of different CAM therapies, their potential risks to the patients, and so on to characterise the effectiveness of such treatment modalities. They, however, do not recommend the use of any such unless their safety and efficacy has been established by current standards [119]. In the United Kingdom, The House of Lords' Select Committee on Science and Technology's report on CAM recommended statutory regulation of CAM practitioners and recommended regulatory bodies of healthcare professionals to develop guidelines on CAM competence and training. By this regulation, conventional healthcare professionals are expected to have a basic knowledge of such therapies, and conventional health providers may have interactions with state registered CAM practitioners [120].

Concerns with Other CAM Therapies

Homoeopathy, for example, even though accepted widely, the methodological quality of the trials based on this system of therapy is found to be very poor. Arguments are still on in the view whether homoeopathy is superior to the placebo as

a treatment concept [121–123]. Adverse effects can occur if the remedies are not highly diluted since most but not all homoeopathic remedies are devoid of active molecules. Many of the homoeopathic prescriptions include remedies containing arsenic or other highly poisonous substances, and in case such a remedy is used in its undiluted form by any chance, it could result in life-threatening consequences [124]. Therapies involving mechanical techniques might cause detrimental effects. Chiropractors, for example, apply a controlled force to a spinal joint and can cause vertebral arterial dissection after upper spinal manipulation [125]. Acupuncture (stimulate specific points on the body by inserting thin needles through the skin) can cause complications like pneumothorax [126, 127], cardiac tamponade [128–130], and central nervous system injuries [131]. Serious infectious complications (like hepatitis, HIV, subacute bacterial endocarditis, etc.) can also arise when the practitioners are not concordant with aseptic techniques [132, 133].

Impact of CAM on Diabetes Treatment Outcomes

In a recent survey conducted among participants of SEARCH for Diabetes in Youth, patients who followed a 'CAM diet' reported a better quality of life (QOL), whereas supplement use and stress reduction activities resulted in decreased QOL. Moreover, children who did not follow any CAM practices experienced lesser treatment barriers [134]. In another study among patients with T2DM and/or cardiovascular disease, higher CAM use was to be highly correlated with a decreased quality of life in. This was attributed to the negative effects of using multiple therapies where some of them could, in fact, interfere with conventional care [135]. CAM use was also found to decrease the adherence towards prescribed medications in different patient populations [136] including those with diabetes. Patients with T2DM who used CAM were almost 6.16 times less adherent to their prescribed diabetes medication than the non-CAM-using counterpart [137, 138]. One of the major reasons postulated towards this diminished adherence is that CAM users are both logistically and psychologically burdened and may need to sacrifice part or all of their prescribed diabetes medication so as to continue using CAM. Another reason pointed out was that the patients believed in CAM healers more than the conventional practitioners [136].

In spite of branding 'natural' and a long history of use, most of these traditional medicines are not necessarily safe. As noted earlier, use of CAMs may delay the use of effective modern conventional treatments and cause adverse effects. Health risks can arise from issues such as drug-herb interactions, adulteration of the products, or presence of inappropriate amounts of active ingredients in the products etc.

[65–67]. Diabetic patients frequently undergo treatment for associated diseases such as hypertension, neuropathy, cardiovascular disease, and such. While evaluating the effect of CAMs, it is important to understand drugs and drug interactions in depth, and the failure to record the present history of CAM use may lead to problems with other medicines that the patient uses [65, 139]. Instances such as renal failure with the use of the dietary supplement chromium picolinate, hepatotoxicity with ingestion of sheep bile, and poor outcomes in a group of patients after abrupt stopping of insulin injections to initiate various CAM therapies have been documented [140]. Another very common drawback noted with CAM products used in diabetes is that when combined with insulin or secretagogues, the patient may experience additive hypoglycaemia due to drug interactions [53]. Herbal medications that claimed to treat diabetes were found to illegitimately incorporate modern medicines with chlorpropamide [141], glibenclamide [142], etc. with a view to enhancing their efficacy and finally resulted in undesirable outcomes. Lead poisoning from herbal remedies is another grave concern [143, 144]. Furthermore, CAM practitioners, as well as manufacturers of such ethnic herbal remedies, even provide patients with fatal advice such as urging them to stop all medicines of diabetes and injections while following CAM therapies which makes the situation even worse [142, 145]. Nutritional advice and lifestyle modifications form essential components of diabetes management,

and such recommendations are also often prescribed by many of the CAM providers. The risk lies with the fact that such advice often differs from those endorsed by conventional diabetes care providers and even does not adhere to the guidelines of ADA for diabetes management. Whether these additional nutritional advice and lifestyle diets complement and reinforce ADA guidelines or conflict with conventional system is another matter of debate [55]. American Diabetes Association's Standards of Medical Care do not support the use of vitamin, mineral, or herbal supplements for diabetes management, due to the lack of sufficient evidence [146].

Several systematic reviews have been published that weighed the impact and efficacy of various CAM therapies on preventing and treating diabetes. Recently, the effect of Ayurveda on treating diabetes mellitus was studied by Sridharan et al., and effect of Chinese herbal medicines on impaired glucose tolerance or impaired fasting blood glucose was assessed by Grant et al. Both these reviews pointed out the benefits of following these traditional systems of medicine in treating diabetes or prediabetic conditions. The authors, however, stop short of recommending such practices citing the biased nature of certain studies and lack of sufficient evidence [99, 147]. An overview of beneficial and adverse effects identified with some of the widely used herbs, herbal products, and supplements for diabetes management is provided in Table 64.3.

Table 64.3 Commonly used herbs and supplements for diabetes management [53, 64, 69, 95, 148–151]

Name of herb, herbal product, or supplement	Beneficial effects/hypothesised mechanism of action	Side effects/drug interactions and contradictions
<i>Cinnamomum zeylanicum</i>	Increases insulin sensitivity by increasing PPAR (alpha and gamma) expression, increases cellular glucose entry by enhanced insulin receptor phosphorylation and translocation of GLUT4 glucose transporter to the plasma membrane, promotes glycogen synthesis	Skin irritations if used topically; interacts with secretagogues and causes hypoglycaemia; coumarins possess anticoagulant, carcinogenic, and hepatotoxic properties
<i>Gymnema sylvestre</i>	Insulin secretagogue; increases glucose uptake promoting enzymes; stimulates and increases beta cell number	May cause hypoglycaemia when combined with secretagogues
Bitter melon (<i>Momordica charantia</i>)	Hypoglycaemic action; insulin mimetic; enhances glucose uptake by tissues; inhibition of glucose-producing enzymes; enhances glucoseoxidation (G6PDH pathway)	Gastrointestinal discomfort, hypoglycaemic coma, favism, haemolytic anaemia in persons with G-6PDH deficiency, abortifacient activity of α and β momorcharin, hypoglycaemia when used with sulfonylureas
Fenugreek (<i>Trigonella foenum-graecum</i>)	Insulin secretagogue; hypoglycaemic activity; lipid-lowering effects; increases HDL cholesterol; slows carbohydrate absorption and delays gastric emptying; inhibits glucose transport; increases insulin receptors; improves utilisation of peripheral glucose	Diarrhoea, gas, uterine contractions, allergic reactions, drug interaction with hypoglycaemic agents, anticoagulant drugs, MAO inhibitors, contraindicated in pregnancy
Guar gum	Alters gastrointestinal transit and delays glucose absorption; lipid-lowering effects by decreasing its absorption and increasing bile excretion	Gastrointestinal upset; may delay the absorption of drugs; possibility of hypoglycaemia when combined with secretagogues; additive lipid lowering when used along with antihyperlipidemic agents

(continued)

Table 64.3 (continued)

Name of herb, herbal product, or supplement	Beneficial effects/hypothesised mechanism of action	Side effects/drug interactions and contradictions
Chromium	Lipid-lowering effects; insulin-sensitising effect by decreasing tyrosine phosphatase activity or direct effect on insulin receptor by increasing tyrosine kinase activity at the insulin receptor; may promote glucose transport	Renal toxicity and dermatological reactions; potential hypoglycaemia with secretagogues; steroids may decrease chromium levels; vitamin C may increase chromium absorption
Alpha-lipoic acid	Improves insulin resistance and increases glucose effectiveness	Can affect thyroid function in patients with thyroid disease; might produce allergic skin reactions, abdominal pain, nausea, vomiting, diarrhoea, and vertigo
Omega-3 fatty acid/fish oil	Lowers triglycerides; anti-inflammatory; anti-platelet; hypotensive; slight increase in blood glucose	High intake might cause bleeding; fish meat to be eaten with caution due to contamination with high levels of methyl mercury; may increase LDL; drug interactions with anticoagulant; and anti-hypertension drugs

Evidence regarding the use of other systems of CAM for diabetes is also in its infancy, and in fact, the available little evidence cautions the patients and the practitioners regarding their safe and effective use. Studies assessing acupuncture are methodologically problematic mainly due to reasons such as the procedure having no adequate control condition, treatments in daily practice being mostly individualised, short duration of the studies, etc. [152–154]. None of the trials conducted in diabetes patients could provide convincing evidence on acupuncture for treating conditions like insulin resistance [154], diabetic gastroparesis [155], and diabetic peripheral neuropathy [156]. Practitioners and patients who support acupuncture for diabetic neuropathy may also bear in mind the increased risk of acupuncture needle site infection with high blood glucose levels [157]. Opting for acupuncture after discontinuing conventional therapy recently led to the death of a 30-year-old T1DM individual in India [158]. ‘Sweet therapy’ is another peculiar diabetes treatment practised in Kerala, which claims to stimulate the sleeping pancreas to secrete insulin by intake of glucose-rich foods such as sweet desserts. However, the long-term serious implications of such modalities on the health of the patients are not documented.

Trials that investigated the effects of tai chi [159–163] and qi gong [152, 164] on diabetes also could not reach any definitive conclusions. Such mind-body therapies which involve movements can at best be considered as alternative modes of exercise [165, 166]. Perceived advantage of these therapies is that they can be performed at almost any level of exercise tolerance when compared to traditional exercise and thus might be helpful for increasing movement and activity especially for some persons with diabetes such as older and obese individuals [152]. They might also be helpful in imparting behavioural and psychological changes and thereby help patients to cope with the disease and increase their quality of life [167]. However, neither yoga [168, 169] nor tai chi [170–172] has been shown to have any significant impact on improving the glycaemic status. In diabetes patients who follow practices such as massage; Therapeutic Touch, Healing Touch, and Reiki; appropriate blood glucose monitoring; and

titration of antidiabetes medications should be recommended when blood glucose levels become lower as pain and discomfort decrease. During energy therapy, catecholamines like epinephrine and norepinephrine get released which can increase lipolysis and thermogenesis, leading to increasing energy expenditure and weight changes [157].

Recommendations for a Prospective CAM Use

Proper Patient-Physician Fit and Judicious Choice of Therapies

The current hypothesis is that treatment settings influence a patient’s mindset and even influence the effects of interventions. This speaks volumes regarding the importance of maintaining a positive relationship between patient and the carer in achieving commendable treatment efficacy [121]. Unfortunately, most of the times, patients following conventional medicine were dissatisfied with the manner of communication by the practitioners, were worried about side effects of pharmacotherapy, and also felt the lack of a holistic treatment approach. On the other hand, CAM seemed to reinforce a patient’s own self-healing capacity. Alternative therapists tend to spend more time with their patients which help to develop a good patient-physician fit, and many of the patients appreciated this approach [173].

CAM use often remains under-reported, and thus a lack of proper communication between patients and healthcare provider can often end up in treatment failures or adverse events. Care providers should put in their efforts to understand the motivations behind a patient’s CAM use and be prepared to counsel such patients, when needed, about the options available and should be able to assess as well as present information to the patients regarding the expected risks, side effects, benefits, and choices regarding self-management and its cost to the patient, helping them to make an informed choice [53, 136, 174]. In patients who persist on following

CAM, it is advisable to identify the effects of each of the components of these medications so that patients can be counselled regarding any contraindications to any of the constituents. Patients should be adequately monitored and warned of the potential side effects, and healthcare practitioners should be aware of the potential interactions between the active components of the alternative medications and other prescribed medications [175]. For individuals exploring supplements, FDA's documents such as 'Tips for the Savvy Supplement User', 'Tips for Older Dietary Supplement Users', 'Questions and Answers on Dietary Supplements, etc. might turn helpful (accessible at <http://www.fda.gov>). A database of natural medicine available at 'www.prescribersletter.therapeuticresearch.com' provides necessary information regarding the usage of herbs and supplements and their safety issues [176]. The American Diabetes Association in two of its articles – 'A Step-by-Step Approach to Complementary Therapies' and 'Guidelines for Using Vitamin, Mineral, and Herbal Supplements' – has offhandedly acknowledged the popularity of CAM for diabetes and provides a set of approaches that could be undertaken in order to safely integrate complementary therapies into an individual's healthcare plan [177, 178]. In its position statement, ADA proposes to evaluate each questionable diagnostic or therapeutic modalities and recommends to provide new and innovative, but unproven, diagnostic and therapeutic measures for patients based on certain preset criteria and also encourage the healthcare providers to ask patients about their alternative therapy practices [179].

Proper Regulations and Well-Conducted Research

Although antidiabetic drugs used in modern medicine have a natural origin [34], administering them in their natural form may not be of much benefit. Randomised clinical trials of herbal medicine interventions too often under-report the crucial characteristics of the intervention, thereby deviating from the standards set by Consolidated Standards of Reporting Trials (CONSORT) [180, 181]. However, with regulated research, there is a higher probability that many more of the natural agents could be used in modern medicine. Experts recommend that CAM and dietary supplements should be subject to a scrutiny similar to conventional medicines by organisations such as the NIH and FDA. Any measure to bypass these may render the healthcare system inefficient, incapable, and dangerous [182, 183]. Adequate or accepted research methodology for evaluating these healthcare practices need to be developed. Consideration should also be given to increase the overall quality of research, avoid publication bias, protect intellectual property, and also certify authentic CAM products and practices from illegitimate ones [184].

Table 64.4 Recommendations for a prospective CAM use

Developing a proper patient-physician fit that can encourage patients to openly communicate regarding CAM use:
Healthcare providers should try to understand patient's motivations behind CAM use so as to choose an optimal treatment plan
Healthcare providers can take efforts to assess, as well as present necessary information to the patients regarding different aspects of CAM use and thus help them make a more informed choice
Validating the safety and efficacy of CAM therapies through well-planned clinical trials that meet quality research standards
Impose proper regulations and scrutiny on CAM practices, products, and practitioners to ensure their safety, quality, and efficacy
Integration of CAM and conventional medical systems by giving emphasis to patient's expectations and needs, without altering the accepted standards of medical and scientific principles.

Integrating CAM into Conventional Care

Although CAM practices lack sufficient evidence, the popularity of such practices is ever increasing, and its integration into mainstream healthcare is much looked at. In certain regions, CAM practices are included under health insurance coverage, and certain 'integrated' delivery systems have also been established [15, 185]. While considering the integration of medical systems, apart from emphasizing patient's expectations and needs, it should be prioritised that accepted standards of medical and scientific principles of practice remain unaltered [186]. With such integration, patients are believed to get benefited at multiple levels such as better decision-making, enhanced physical and emotional well-being, and gaining knowledge on health-promoting practices (Furnham, 1996). Healthcare providers can also get benefitted in terms of greater satisfaction through learning new treatment strategies and developing skills to implement them [187]. Thus a more integrated system is expected to facilitate discussion and collaboration between the two systems of medicine to improve healthcare delivery [188]. A snapshot of the recommendations suggested towards a prospective CAM use is provided in Table 64.4.

Conclusion

Even with the advancements achieved in modern conventional medicine, a lot many patients still continue to follow traditional CAM practices due to a variety of reasons such as their perceived safety and efficacy, easy availability or matching with their cultural beliefs and practices, and so on. However, the risk-benefit ratio of these CAM practices on the disease outcomes especially the chronic ones like diabetes still remains unproven. Conventional healthcare providers in most of the cases are not aware of their patients following such modes of therapies and also are not in a position to comment on regarding the same. They should put in efforts to maintain a good rapport with the patients so as to

enable an open communication regarding CAM use so as to help them make a judicious choice of such therapies. Imposing stringent rules and regulations as well as conducting clinical trials that meet quality research standards can in no doubt reveal the true potential of at least some of these age-old practices. With that achieved, a successful integration of reliable and safe CAM practices into mainstream healthcare can be thought of in order to improve the overall treatment experience and outcomes.

Multiple-Choice Questions

1. Complementary and alternative medicines:
 - (a) Are essential additional elements of diabetes management
 - (b) Are healthcare approaches developed outside the realm of conventional medicine
 - (c) Are exclusively medicines
 - (d) Include surgical interventions
 - (e) Are evidence-based
2. Complementary health approaches:
 - (a) Are rarely used
 - (b) Are largely used by people with low economic resources
 - (c) Are used by 33.2% of adults in the United States
 - (d) Are used mostly by men
 - (e) Represent a minimal amount of healthcare costs
3. Reasons for the popularity of complementary alternative medications include all of the following, except:
 - (a) Easy accessibility
 - (b) Dissatisfaction with conventional medical care
 - (c) Belief of safety
 - (d) High costs
 - (e) Poor doctor-patient relationship
4. Many currently approved antidiabetic medications have a natural origin.
 - (a) True
 - (b) False
5. Examples of antidiabetic drugs with natural origin:
 - (a) Insulin
 - (b) Sulfonylureas
 - (c) Metformin
 - (d) SGLT2 inhibitors
 - (e) GLP-1 agonists
6. The percentage of patients with type 2 diabetes using complementary medicine in addition to conventional prescriptions:
 - (a) 15%
 - (b) 27%
 - (c) 48%
 - (d) 60%
 - (e) 77%
7. The use of complementary alternative medications has several risks, including:
 - (a) Adverse effects
 - (b) Hidden costs
 - (c) Overload with unsuccessful therapies
 - (d) Lack of proper regulations
 - (e) All of the above
8. The hypothesised mechanism of action of chromium:
 - (a) Insulin secretagogue
 - (b) Insulin sensitising agent
 - (c) Insulin mimetic
 - (d) Inhibits glucose transport
 - (e) Alters gastrointestinal transit
9. The hypothesised mechanism of action of guar gum:
 - (a) Insulin secretagogue
 - (b) Insulin sensitising agent
 - (c) Insulin mimetic
 - (d) Inhibits glucose transport
 - (e) Alters gastrointestinal transit
10. Recommendations for the prospective use of complementary alternative medications involve:
 - (a) Recognition as essential elements of management
 - (b) Learning about their effectiveness
 - (c) Judicious choice of therapies
 - (d) Combination with standard therapies
 - (e) Discourage their use by patients

Correct Answers

1. (b) Are healthcare approaches developed outside the realm of conventional medicine
2. (c) Are used by 33.2% of adults in the United States
3. (d) High costs
4. (a) True
5. (c–e)
6. (e) 77%
7. (e) All of the above
8. (b) Insulin sensitising agent
9. (b and e)
10. (c) Judicious choice of therapies

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