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# Original article

# Prevalence of complementary and alternative medicine use among rheumatoid arthritis patients in Saudi Arabia



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#### ABSTRACT

Background and aim: The use of complementary and alternative medicine (CAM) is unexplored among Saudi rheumatoid arthritis (RA) patients. The aim of this study was to estimate the prevalence and types of CAM used among patients with RA and factors associated with their use.

Experimental procedure: A cross-sectional study was conducted at rheumatology clinics in two tertiary hospitals located in Riyadh, Saudi Arabia. The data was collected between May 2017 and February 2018. Unpaired Student's *t*-tests, Chi-square tests, and Pearson correlation tests were used to compare users vs nonusers.

Results: A total of 438 patients (mean age = 49, SD  $\pm$  15 years; 89.7% females) were included in this study. Sixty seven percent of included patients had used CAM for their RA. The majority of CAM users were female (92.1%). The most frequently used CAM products were vitamin D (47%), calcium (37%), honey (15%), ginger (13%), turmeric (11%), black seeds (8%), and fenugreek (8%). One hundred ninety-six (45%) patients believe that CAM is safe, and 287 (96%) patients took it because they believed that CAM had "added benefits". Statistically significant differences were found for gender, RA duration, erythrocyte sedimentation rate (ESR) level, and seropositivity between CAM users and nonusers (P = 0.019, P = 0.011, P = 0.022, and P < 0.0001, respectively). A significant correlation was found between the Erythrocyte Sedimentation Rate (ESR) level, RA duration and CAM use (P = 0.110, P = 0.022 and P = 0.121, P = 0.012, respectively). These data indicated that patients who used CAM had higher ESR level and longer disease duration than patients didn't use CAM.

Conclusion: There is a high prevalence of CAM use among RA patients. CAM use was perceived to add benefit and patients using it had higher ESR. Larger studies are needed to assess the use of CAM and its impact on RA and its management.

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Abbreviations: CAM, complementary and alternative medicine; RA, rheumatoid arthritis; ACR EULAR criteria, American College of Rheumatology and the European League Against Rheumatism; HAQ, health assessment questionnaire; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; RF, rheumatoid factor; Anti-CCP, anti-cyclic citrullinated peptide.

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#### 1. Introduction

Public interest in complementary and alternative medicine (CAM) is becoming increasingly popular worldwide in both healthy individuals and in patients with chronic diseases (Alrowais and Alyousefi, 2017). In many countries, including Saudi Arabia, at least half of the general population uses CAM (United States [US], 82% (Prasad et al., 2013); Australia, 61% (Thomson et al., 2012); Malaysia, 51% (Saibul et al., 2012); Turkey, 61% (Nazik et al., 2012) and Saudi Arabia (Mohammad et al., 2015). CAM is often used concomitantly with prescription drugs for managing chronic conditions, such as chronic pain and arthritis, or more life-threatening

illnesses, such as heart diseases and cancer (Elolemy and Albedah, 2012). The National Center for Complementary and Integrative Health (NCCIH) showed that the musculoskeletal problems such as back, neck, muscles, and joint pain are the most common health conditions promoting CAM use among American by 31.7% (NIH, 2017).

Rheumatoid arthritis (RA) is the most common form of inflammatory arthritis and is associated with an increased burden on individuals and healthcare systems (Singh et al., 2016). It was reported that more than half of the population with this illness attempt to manage it with CAM products (Thomson et al., 2012). This high rate of CAM use by patients with RA, may reflect that pain is the primary motivation (Efthimiou et al., 2010). In addition, the desire to try every available treatment, the willingness to take control of illness, and the incorrect notion that CAM doesn't carry any harm are relevant factors (Efthimiou et al., 2010). It is commonly held that patients choose to use CAM because they are dissatisfied with conventional agents that they consider to be ineffective or dangerous (Efthimiou et al., 2010). However, disappointment with conventional agents is not necessarily the reason why patients turn to CAM (Efthimiou et al., 2010).

CAM practices vary across countries depending on prevalent traditions and the definition of CAM. In Western countries, the most commonly used types of CAM include relaxation techniques, medical massage therapy, acupuncture, yoga, meditation, and the consumption of ginseng and mineral supplements (Clarke et al., 2015). However, in Saudi Arabia, CAM practices are mostly related to cultural and religious beliefs. Common practices in Saudi Arabia, such as the use of honey, camel milk, Zamzam water, olive oil cupping, and skin cauterization are often based on Quranic traditions and Sunnah (the body of advice and teachings of Prophet Muhammad, peace be upon him) (Al-Zahim et al., 2013; Mohammad et al., 2015).

In Saudi Arabia and due to the strong believes related to CAM use, a center for complementary and alternative medicine was established by a ministerial decree (No. 236) date 10/8/1429H (12/8/2008 G). The objectives of the center is to be a reference center for all matters related to CAM, to regulate CAM practices within the health-care services, and to use evidence based CAM in addition to conventional medicine (NCCAM, 2008).

Further more to all previously discussed factors, studying the patterns and prevalence of CAM use is important because sufficient evidence supporting its safety is currently lacking. This information is especially important in the context of chronic diseases and polypharmacy. Several published reports have highlighted serious adverse events and potential herb-drug interactions (Setty and Sigal, 2005; Shaw et al., 1997; Williamson, 2003). Fourteen diabetic patients who were prescribed lamb bile by a local CAM practitioner in Saudi Arabia suffered from adverse events, and 12 of these patients were hospitalized after they consumed it (Al-Qahtani, 1996).

Practitioners face another dilemma in regard to CAM. According to a survey published in 2013 in the US, only 14.4% of patients informed their physicians about their CAM use (Prasad et al., 2013). Likewise, a household survey published in 2012 in Saudi Arabia reported that only 8.3% of patients discussed their CAM use with their physician (Elolemy and Albedah, 2012). Thus, with the influence of the Quran and Sunnah, the Saudi population with RA is expected to hold strong and unique beliefs regarding CAM use. The aim of this study was to determine the prevalence of CAM use among patients with RA, to identify the most commonly used types of CAM and factors associated with their use.

#### 2. Materials and methods

#### 2.1. Study design and settings

A cross-sectional study guided by the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) checklist for cross-sectional studies was conducted (Von Elm et al., 2007). The study was performed in the rheumatology clinics of two tertiary hospitals. Both hospitals were referral centers; one was an academic and teaching center with a bed capacity of 1200 and the other was a military hospital with the same bed capacity, and both were located in Riyadh, Saudi Arabia. The study survey was conducted between May 2017 and February 2018. Patients who were at least 18 years of age with a clinically documented diagnosis of RA based on the 2010 American College of Rheumatology/European League Against Rheumatism (2010 ACR EULAR) criteria (Aletaha et al., 2010) for at least 3 months and were able to respond to the surveyors were recruited.

Ethical approval was granted from both hospitals prior to study inclusion by the Institutional Review Boards (project number E-17-2392 and HAP-01-R-015, respectively). All the patients signed an informed consent form.

#### 2.2. Data sources and measurements

No fixed definition is available for CAM, so like Anderson et al. (2000) we defined CAM as "any product, including herbal remedies, vitamins, minerals, and natural products, which may be purchased without a prescription for the purpose of self-treatment" in this study.

The data sources for the project were two-fold, namely patient interviews and medical chart reviews. The patients were interviewed using a survey in their native Arabic language that was developed by the investigators. The survey was subjected to face validity were it was sent to expert in the field of pharmacognosy and alternative medicine. The survey was then piloted on a group of rheumatoid arthritis patients for clarity of contents. Demographics, clinical and biochemical data were collected using a standardized data collection sheet.

# 2.3. Component 1: Patient interview

#### 2.3.1. Questions on CAM

The questions addressed the type of CAM taken since disease diagnosis; sources of information about CAM products; locations where CAM was obtained; and patient knowledge about the relative safety of the products and reasons for CAM use (Anderson et al., 2000; Thomson et al., 2012).

#### 2.3.2. Income level

All the patients were asked about their average monthly income. Low income <5000 SR, intermediate income 5000–10,000 SR, and high income >10,000 SR.

# 2.3.3. Health assessment questionnaire (HAQ) for subjective disease activity measurement

A reliable and valid Arabic version of HAQ for measuring functional disability in Arabic-speaking patients with RA was used (El Meidany et al., 2003). The HAQ scores range from mild (HAQ 0–1) to moderate (HAQ < 1–2) and severe functional disability (HAQ < 2–3).

#### 2.3.4. Likert scale regarding perceived safety concept

All the patients were asked to indicate their level of agreement with a given statement that "complementary and alternative medicines are safe" (Anderson et al., 2000). The answers were recorded on a five-point Likert scale ranging from "Strongly Disagree" to "Strongly Agree" (Mcleod et al., 2011).

2.4. Component 2: Medical chart review using the eSihi and DORTAL electronic hospital health information system for collecting data

## 2.4.1. Patient demographics

Patient age, nationality, weight, height, and body mass index (BMI) were recorded.

#### 2.4.2. Social status

Patient marital status, occupation, and residence were recorded.

#### 2.4.3. Education level

Patients were marked as being illiterate or having an elementary, high school, diploma, university degree, or postgraduate degree.

#### 2.4.4. Laboratory information

Test results were collected within one week (±1 week) of the patient interview for the following parameters: the erythrocyte sedimentation rate (ESR); C-reactive protein (CRP), and rheumatoid factor (RF).

#### 2.5. Statistical analysis

The analysis was conducted using the Statistical Package for Social Sciences (SPSS) for Windows, version 22. Based on average prevalence of 64%, 95% confidence interval, 0.05 precision and adding 20%, the calculated sample size was 424. Statistical comparisons were made between CAM users and nonusers. Means and standard deviations were used to describe continuous variables. Frequencies and proportions were used for describing categorical variables. Unpaired Student's *t*-tests were used to assess significant differences between the means of the groups. A Chi-square test was used for categorical data. A Pearson correlation test was used to explore correlations between continuous variables and CAM use. The significance level of 0.05 was adopted for all the statistical tests.

# 3. Results

# 3.1. Prevalence

Four hundred thirty-eight patients completed the survey/interview, signed consent and were included in the final study analysis. The mean ( $\pm$ SD) age of the patients was 49 ( $\pm$ 15) years. The majority of included patients, were female (89.7%), of Saudi descent (98.2%) and resided in Riyadh (74.2%). Table 1 shows the demographic characteristics of the CAM users and non-users. The mean ( $\pm$ SD) age of the CAM users was 49 ( $\pm$ 14) years, which was comparable to that of non-users 48 ( $\pm$ 16) years (P = 0.528). The mean ( $\pm$ SD) BMIs were similar in both groups (P = 0.720).

Two hundred ninety-two (66.7%) individuals had used CAM. The mean ( $\pm$ SD) RA duration was longer in CAM users at 11 ( $\pm$ 8) years compared to 9 ( $\pm$ 7) years in nonusers (P = 0.011). The CAM users were commonly illiterate (71 patients; 24.3%), while the most common education level in non-users was a postgraduate degree (43 patients; 29.5%). CAM was more frequently used by patients with an intermediate income 5000–10,000 SR (37.6%),

**Table 1** Demographics and baseline characteristics (N = 438).

Demographic	CAM users (N = 292)	Non-users (N = 146)	Total (N = 438)
Female gender (%)	269 (92.1)	124 (84.9)	393 (89.7)
Age (years), Mean (±SD)	49 (±14)	48 (±16)	49 (±15)
Seropositive (%)	162 (82.2)	65 (64.4)	227 (76.2)
BMI (kg/m²), Mean (±SD)	30.55 (±6.73)	30.28 (±7.36)	30.46 (±6.94)
Duration of having RA	11 (±8)	9 (±7)	10 (±8)
(years), Mean (±SD)			
Saudi nationality (%)	288 (98.6)	142 (97.3)	430 (98.2)
Riyadh residence (%)	218 (74.7)	107 (73.3)	325 (74.2)
Marital status (%)			
Single	41 (14)	26 (17.8)	67 (15.3)
Married	198 (67.8)	100 (68.5)	298 (68)
Divorced	24 (8.2)	4 (2.7)	28 (6.4)
Widowed	29 (9.9)	16 (11)	45 (10.3)
Education (%)			
Illiterate	71 (24.3)	34 (23.3)	105 (24)
Elementary school	56 (19.2)	22 (15.1)	78 (17.8)
High school	62 (21.2)	22 (15.1)	84 (19.2)
Diploma	36 (12.3)	19 (13)	55 (12.6)
University degree	5 (1.7)	6 (4.1)	11 (2.5)
Postgraduate degree	62 (21.2)	43 (29.5)	105 (24)
Employed (%)	64 (21.9)	32 (21.9)	96 (21.9)
Monthly income (%)			
Low <5000 SR	89 (30.5)	35 (24)	124 (28.3)
Intermediate 5000-10,000 SR	110 (37.6)	61 (41.8)	171 (39)
High >10,000 SR	93 (31.8)	50 (34.2)	143 (32.6)
ESR (mm/hr) (±SD)	28 (±21)	24 (±20)	27 (±21)
CRP (mg/L) (±SD)	8 (±12)	9 (±11)	8 (±11)
HAQ score 0-3 (±SD)	1.14 (±0.82)	1.09 (±0.81)	1.12 (±0.82)
Pain score 0–100 (±SD)	42 (±31)	45 (±31)	43 (±31)
Morning stiffness (%)	129 (44.2)	61 (41.8)	190 (43.4)

SD: Standard deviation, Seropositive (which indicates either RF: Rheumatoid factor or Anti-CCP: Anti-cyclic citrullinated peptide), BMI: Body mass index (Kilograms per meter squared), RA: Rheumatoid arthritis, SR: Saudi Riyals, ESR: Erythrocyte sedimentation rate (Millimeters/hour), CRP: C-reactive protein (Milligram/liter), HAO: Health assessment questionnaire.

compared with those with high >10,000 SR (31.8%) and low incomes <5000 SR (30.5%) (P = 0.154).

The mean ( $\pm$ SD) ESR, CRP, and pain score in CAM users were 28 ( $\pm$ 21 mm/hr), 8 ( $\pm$ 12 mg/L), and 42 ( $\pm$ 31), respectively. The mean ( $\pm$ SD) HAQ score in CAM users was 1.14 ( $\pm$ 0.82). In CAM users, seropositive results were found in 162 (82.2%) patients. Morning stiffness (that lasts at least an hour) among CAM users was found in 129 (44.2%) patients. On the other hand non-users had significantly lower ESR 24 ( $\pm$ 20), comparable CRP 9 ( $\pm$ 11), comparable pain score 45 ( $\pm$ 31) and HAQ score 1.09 ( $\pm$ 0.81). Non-users had significantly lower seropositivity 65 (64.4%) than CAM users. Regarding morning stiffness non-users had lower occurrence 61 (41.8%) but was not significant. Table 1 shows baseline demographics and information related to RA in CAM users versus non-users.

The most frequently used herbal or plant-derived products were honey, used by (15%), ginger by (13%), turmeric by (11%), black seeds by (8%), and fenugreek by (8%). The most frequently used minerals and vitamins were vitamin D by (47%), calcium by (37%) and multivitamins by (8%) (Fig. 1 illustrate different herbal-supplements used by participants).

Of the 292 RA patients who used CAM, (96%) took them because they believed CAM had "added benefits" (Table 2 has reasons for CAM use among participants). The places where patients most frequently obtained CAM products are summarized in Table 2. Most of the patients purchased herbal or plant-derived products from the apothecary, as purchased by (29%) of patients and health food stores, by (14%) of patients. Over-the-counter minerals and vitamins were obtained from pharmacies by (56%).

The primary source of information about herbal products was family, relatives and friends with (34%) respondents and social

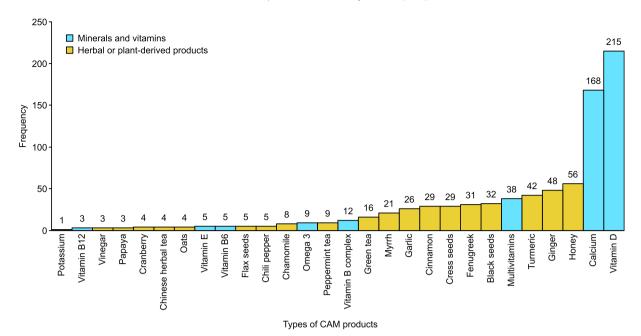


Fig. 1. Most commonly used CAM products.

**Table 2** Exploring different reasons, purchase sites, and information sources for the use of complementary and alternative medicine (n = 292).

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Reason	Number (%)
Reasons for using complementary and alternative medic	cine (%)
Unsatisfied with conventional disease management	9 (3)
Added benefits	287 (96)
Distrust of conventional disease management	1 (0)
Other	3 (1)
Sites where patients purchased complementary and alte (%)	rnative medicine
Health food store	65 (14)
Pharmacies	259 (56)
Online	5 (1)
Apothecary	131 (29)
Source of information regarding complementary and alte (%)	rnative medicine
Friends or family members	101 (34)
Pharmacists	133 (45)
Medical doctor	2(1)
Social media	57 (19)
Television	1 (0)
Advertisements	2(1)

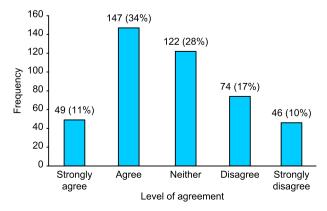


Fig. 2. Likert scale to perceived safety concept about CAM products.

media, with (19%) (Table 2 shows source of information for CAM products). However, the primary source of information about minerals and vitamins was pharmacists at (45%). One hundred ninetysix patients (45%) agreed that CAM was safe (Fig. 2 illustrates patients safety perception of CAM products).

## 3.2. Correlations and comparisons

The groups did differ significantly in terms of gender and RA duration (P = 0.019 and P = 0.011, respectively). Additionally, CAM users and nonusers showed statistically significant differences with respect to their ESR level and to being seropositive (P = 0.022 and P < 0.0001, respectively). A significant correlation was found between CAM use and both the ESR and RA duration (r = 0.110, P = 0.022 and r = 0.121, P = 0.012, respectively). Other continuous variables such as age, HAQ score, pain score, and CRP were not correlated with CAM use. These data indicated that

**Table 3**Bivariate analysis of demographic features and laboratory results specific for RA using Chi-square tests and unpaired Student's *t*-tests, as appropriate (N = 438).

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Variables	P-value
Gender; male or female	0.019
Age (years)	0.528
Seropositive	<0.0001
BMI (kg/m <sup>2</sup> )	0.720
Duration of having RA (years)	0.011
Marital status	0.885
Education	0.812
Monthly income	0.154
ESR (mm/h)	0.022
CRP (mg/L)	0.802
HAQ score 0–3	0.605
Pain score 0–100	0.369
Morning stiffness	0.633

Seropositive (which indicates either RF: Rheumatoid factor or Anti-CCP: Anti-cyclic citrullinated peptide), BMI: Body mass index (Kilogram per meter square), RA: Rheumatoid arthritis, ESR: Erythrocyte sedimentation rate (Millimeters/hour), CRP: C-reactive protein (Milligram/liter), and HAQ: Health assessment questionnaire; Statistically significant (p < 0.05) variables are noted in bold font.

CAM use increased with elevated ESR and longer disease duration (Table 3).

No statistically significant differences were found between CAM users and non-users in relation to their age, marital status, education, and monthly income (P = 0.528, P = 0.885, P = 0.812, and P = 0.154, respectively). No statistically significant difference was found for CRP, HAQ score, pain score, and morning stiffness between these groups (P = 0.802, P = 0.605, P = 0.369, and P = 0.633, respectively) (Table 3).

#### 4. Discussion

The current study has higher figures than the some calculations for western RA patients. Herman et al. (2004) reported that the proportion of RA patients who used CAM was 17.3% in Mexico. Thomson et al. (2012) found that 61% of Australian RA patients used self-prescribed CAM. This difference in prevalence between our study and other western studies could be explained by various factors, such as different population characteristics, beliefs, and traditions in addition to different definitions of CAM. However, in 2015, Mohammad et al. (2015) reported that the prevalence of CAM use in the general Saudi population was 67%, which was similar to what we found.

In the present study, female patients used CAM more frequently than male patients, and the difference was statistically significant (P = 0.019). These results were in accordance with the findings Alwhaibi and Sambamoorthi (2016) were a significantly higher percentage of women have ever used CAM (51.5%) with an adjusted odds ratio of = 1.49 (95% CI = 1.35–1.65). The most frequently used types of CAM in the current study were honey, ginger, turmeric, black seeds, fenugreek, vitamin D, calcium, and multivitamins. This finding was consistent with Al-Zahim et al. (2013) who found that honey, black seeds, anise, green tea, and myrrh were the most frequently used CAMs. By contrast, in western countries, the seven best-selling herbal medicines were Ginkgo biloba, St. John's wort, grape seeds, ginseng, garlic, cranberries, and kava (Anderson et al., 2000; Gardiner et al., 2007).

Family, relatives, friends and social media were the common sources of advice and recommendations about CAM among RA patients, while the primary source of information about minerals and vitamins were pharmacists. This result has also been reported by Elolemy and Albedah (2012), in which mass media (e.g., T.V., newspapers, and radio) and family, relatives and friends served as the primary sources of CAM knowledge. In fact, Naidu et al. (2005) reported that pharmacists do not perceive natural health products (NHPs) (including vitamins, minerals, and herbal remedies that are available as over-the-counter products for self-care) to be the same as conventional medications, and they are less knowledgeable about NHPs than about prescribed medications. Similarly, Olatunde et al. (2010) highlighted a professional dilemma faced by pharmacists when they work in a pharmacy that provides NHPs and they do not have sufficient knowledge to answer questions about these products. Thus, it is important for pharmacists to have a basic level of knowledge about the NHPs sold in their pharmacies to counsel their patients.

The high rate of CAM use by our patients was to add benefit to conventional treatment. It was apparent that patient in the CAM user group had issues with their illness, which was supported by the significantly high ESR, slightly greater morning stiffness, and HAQ score. Palinkas and Kabongo (2000). suggested that popularity of CAM use could be the fear of adverse events from conventional therapy. This could be the drive behind seeking better disease control using alternative measures. Other factors affecting ESR like potential drug-herb interaction, patient non-compliance, response to conventional therapy and its relation to CAM should be

explored. In regards to our finding of greater disease duration and seropositivity among users was in accordance to what was published in the literature (Efthimiou et al., 2010; Majka et al., 2008).

This study strength is that it was the first of its kind exploring the use of CAM products among Saudi RA patients. The current study has limitations. First, it included patients from only two centers in the central region, which could be a source of selection bias and could limit the generalizability of the results. Second, the information provided by the participants could be subject to recall bias.

This study highlight CAM use among RA patients, and thus shows the need to evaluate and control the use of CAM in chronic diseases in general, by governmental agencies, private corporations, and academic institutions. All may consider adopting a more proactive posture concerning the implementation of clinical and basic science research, improving the quality control of dietary supplements, and establishing postmarket surveillance for drugherb interactions. We also encourage pharmacist to lead an active role in patient education with regards to CAM especially in the context of chronic illness.

#### 5. Conclusions

There is a high prevalence of CAM use among RA patients. It is clear that CAM is perceived to be safe by majority of patients and thus they might use them without consulting their physician. This uncontrolled use to add benefit might reflect issues related to disease control and need further exploration. The results of this study although descriptive, should encourage healthcare practitioners to ask patients about alternative therapy, and consider its effect on drug therapy. Further studies are needed to assess the use of CAM, its effect on disease outcome like ESR and its impact on RA management.

# **Author contributions**

Initiated and supervised the work: TMH, HMM. Conducted the experiments: AMM, BAO, MSB.

Participated in research design: TMH, HMM, AMM, AAG.

Analyzed the data: AMM, AAG.

Wrote or contributed to the writing of the manuscript: AMM, TMH, HMM, AAG, MAO, HA, AA.

# **Declaration of Competing Interest**

None.

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#### Appendix A. Supplementary material

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#### References

- Al-Qahtani, M.S., 1996. Hepatic and renal toxicity among patients ingesting sheep bile as an unconventional remedy for diabetes mellitus-Saudi Arabia, 1995.
- MMWR Morb. Mortal. Wkly. Rep. 45, 941–943.

  Aletaha, D., Neogi, T., Silman, A.J., Funovits, J., Felson, D.T., Bingham 3rd, C.O., Birnbaum, N.S., Burmester, G.R., Bykerk, V.P., Cohen, M.D., Combe, B., Costenbader, K.H., Dougados, M., Emery, P., Ferraccioli, G., Hazes, J.M., Hobbs, K., Huizinga, T.W., Kavanaugh, A., Kay, J., Kvien, T.K., Laing, T., Mease, P., Menard, H.A., Moreland, L.W., Naden, R.L., Pincus, T., Smolen, J.S., Stanislawska-Biernat, E., Symmons, D., Tak, P.P., Upchurch, K.S., Vencovsky, J., Wolfe, F., Hawker, G., 2010. 2010 Rheumatoid arthritis classification criteria: an American college of rheumatology/European league against rheumatism collaborative initiative. Arthritis Rheum. 62, 2569–2581. https://doi.org/10.1002/art.27584.
- Alrowais, N.A., Alyousefi, N.A., 2017. The prevalence extent of Complementary and Alternative Medicine (CAM) use among Saudis. Saudi Pharm. J. 25, 306–318. https://doi.org/10.1016/j.jsps.2016.09.009.
- Alwhaibi, M., Sambamoorthi, U., 2016. Sex Differences in the use of complementary and alternative medicine among adults with multiple chronic conditions. Evid. Compl. Alternat. Med. 2016, 2067095. https://doi.org/10.1155/2016/2067095.
- Compl. Alternat. Med. 2016, 2067095. https://doi.org/10.1155/2016/2067095. Al-Zahim, A.A., Al-Malki, N.Y., Al-Abdulkarim, F.M., Al-Sofayan, S.A., Abunab, H.A., Abdo, A.A., 2013. Use of alternative medicine by Saudi liver disease patients attending a tertiary care center: prevalence and attitudes. Saudi J. Gastroenterol.: Off. J. Saudi Gastroenterol. Assoc. 19, 75–80 https://doi:10.4103/1319-3767.108477.
- Anderson, D.L., Shane-McWhorter, L., Crouch, B.I., Andersen, S.J., 2000. Prevalence and patterns of alternative medication use in a university hospital outpatient clinic serving rheumatology and geriatric patients. Pharmacotherapy 20, 958– 966. https://doi.org/10.1592/phco.20.11.958.35257.
- Clarke, T.C., Black, L.I., Stussman, B.J., Barnes, P.M., Nahin, R.L., 2015. Trends in the use of complementary health approaches among adults: United States, 2002–2012. Natl. Health Stat. Rep. 79, 1–16.
- Efthimiou, P., Kukar, M., Mackenzie, C.R., 2010. Complementary and alternative medicine in rheumatoid arthritis: no longer the last resort! HSS J. 6, 108–111. https://doi.org/10.1007/s11420-009-9133-8.
- El Meidany, Y.M., El Gaafary, M.M., Ahmed, I., 2003. Cross-cultural adaptation and validation of an arabic health assessment questionnaire for use in rheumatoid arthritis patients. Joint Bone Spine 70, 195–202. https://doi.org/10.1016/S1297-319X(03)00004-6
- Elolemy, A.T., Albedah, A.M., 2012. Public knowledge, attitude and practice of complementary and alternative medicine in Riyadh region, Saudi Arabia. Oman Med. J. 27, 20–26. https://doi.org/10.5001/omj.2012.04.
- Gardiner, P., Graham, R., Legedza, A.T., Ahn, A.C., Eisenberg, D.M., Phillips, R.S., 2007. Factors associated with herbal therapy use by adults in the United States. Altern. Ther. Health Med. 13, 22–29.
- Herman, C.J., Allen, P., Hunt, W.C., Prasad, A., Brady, T.J., 2004. Use of complementary therapies among primary care clinic patients with arthritis. Preventing Chronic Dis. 1 (4), A12.
- Majka, D.S., Deane, K.D., Parrish, L.A., et al., 2008. Duration of preclinical rheumatoid arthritis-related autoantibody positivity increases in subjects with older age at time of disease diagnosis. Ann. Rheumatic Dis. 67, 801–807 https://ard.bmj.com/content/67/6/801.citation-tools.

- Mcleod, A., Pippin, S., Wong, J., 2011. Revisiting the Likert scale: can the fast form approach improve survey research. Int. J. Behav. Account. Finance 2, 310–327. https://doi.org/10.1504/IJBAF.2011.045019.
- Mohammad, Y., Al-Ahmari, A., Al-Dashash, F., Al-Hussain, F., Al-Masnour, F., Masoud, A., Jradi, H., 2015. Pattern of traditional medicine use by adult Saudi patients with neurological disorders. BMC Compl. Alternat. Med. 15 (1) https://doi:10.1186/s12906-015-0623-6.
- Naidu, S., Wilkinson, J.M., Simpson, M.D., 2005. Attitudes of Australian pharmacists toward complementary and alternative medicines. Ann. Pharmacother. 39, 1456–1461. https://doi.org/10.1345/aph.1G089.
- National Center for Complementary and Integrative Health (NCCIH), 2017.

  Diseases/conditions for which CAM is most frequently used among adults for 2007 and 2002 accessed 26 May 2019 https://nccih.nih.gov/research/
  statistics/2007/diseases-conditions-for-which-cam-is-frequently-used-among-adults
- National Center for Complementary and Alternative Medicine, 2008. Goals and future plan for the national center of complementary medicine center in Saudi Arabia accessed 27 May 2019 http://www.nccam.gov.sa/Home.aspx, .
- Nazik, E., Nazik, H., Api, M., Kale, A., Aksu, M., 2012. Complementary and alternative medicine use by gynecologic oncology patients in Turkey. Asian Pacific J. Cancer Prevent. 13, 21–25 https://doi:10.7314/apjcp.2012.13.1.021.
- Olatunde, S., Boon, H., Hirschkorn, K., Welsh, S., Bajcar, J., 2010. Roles and responsibilities of pharmacists with respect to natural health products: key informant interviews. Res. Social Adm. Pharm. 6, 63–69. https://doi.org/10.1016/j.sapharm.2009.02.004.
- Palinkas, L.A., Kabongo, M.L., San Diego Unified Practice Research in Family Medicine Network, 2000. The use of complementary and alternative medicine by primary care patients. A SURF\*NET study. J. Fam. Pract. 49, 1121–1130.
- Prasad, K., Sharma, V., Lackore, K., Jenkins, S.M., Prasad, A., Sood, A., 2013. Use of complementary therapies in cardiovascular disease. Am. J. Cardiol. 111, 339– 345 https://doi:10.1016/j.amjcard.2012.10.010.
- Saibul, N., Shariff, Z.M., Rahmat, A., Sulaiman, S., Yaw, Y.H., 2012. Use of complementary and alternative medicine among breast cancer survivors. Asian Pacific J. Cancer Prevent. 13, 408–4086 https://doi:10.7314/apjcp.2012. 13.8.4081
- Setty, A.R., Sigal, L.H., 2005. Herbal medications commonly used in the practice of rheumatology: mechanisms of action, efficacy, and side effects. Semin. Arthritis Rheum. 34, 773–784. https://doi.org/10.1016/j.semarthrit.2005.01.011.
- Shaw, D., Leon, C., Kolev, S., Murray, V., 1997. Traditional remedies and food supplements. A 5-year toxicological study (1991–1995). Drug Saf. 17, 342–356. https://doi.org/10.2165/00002018-199717050-00006.
- Singh, J.A., Saag, K.G., Bridges Jr., S.L., Akl, E.A., Bannuru, R.R., Sullivan, M.C., Vaysbrot, E., McNaughton, C., Osani, M., Shmerling, R.H., Curtis, J.R., Furst, D.E., Parks, D., Kavanaugh, A., O'Dell, J., King, C., Leong, A., Matteson, E.L., Schousboe, J.T., Drevlow, B., Ginsberg, S., Grober, J., St Clair, E.W., Tindall, E., Miller, A.S., McAlindon, T., 2016. 2015 American college of rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Rheumatol. 68, 1–26. https://doi.org/10.1002/art.39480.
- Thomson, P., Jones, J., Evans, J.M., Leslie, S.L., 2012. Factors influencing the use of complementary and alternative medicine and whether patients inform their primary care physician. Compl. Therap. Med. 20, 45–53 https://doi:10.1016/j. ctim.2011.10.001.
- Von Elm, E., Altman, D.G., Egger, M., Pocock, S.J., Gøtzsche, P.C., Vandenbroucke, J.P., 2007. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann. Intern. Med. 147, 573–577. https://doi.org/10.1016/S0140-6736(07)61602-X.
- Williamson, E.M., 2003. Drug interactions between herbal and prescription medicines. Drug Saf. 26, 1075–1092. https://doi.org/10.2165/00002018-200326150-00002.