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Review Article

Effectiveness of medicinal herbs on psychological indices before and after surgeriesGholamreza Shabanian¹, Saeid Heidari-Soureshjani^{2*} & Johannes Salcher³¹ Department of Anesthesia, Shahrekord University of Medical Sciences, Shahrekord, Iran² Deputy of Research and Technology, Shahrekord University of Medical Sciences, Shahrekord, Iran³ University of Vienna, Vienna, Austria**Article history**

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Abstract

Psychological complications appear to be significant disorders which need prolonged recovery period. They cause disability and impose hospitalized costs on patients. This systematic review was aimed to investigate the effectiveness of medicinal herbs on psychological indices in patients undergoing surgeries. The keywords such as anxiety, depression, aggressive, impulsive, stress, delirium and cognitive in combination with surgery and medicinal plants search terms such as medicinal plant or phyto or herb were used to search for relevant publications indexed in the Institute for Scientific Information (ISI), Scopus and PubMed using EndNote software. A total of 1231 studies with mentioned keywords were added to the bank of the study and after considering inclusion and exclusion criteria, 36 human studies were reviewed. Some medicinal plants such as *Passiflora incarnata* L., *Valeriana officinalis* L., *Melissa officinalis* L., *Crocus sativus* L., and *Rosa damascena* Mill. and some herbal formulas like Hochu-ekki-to and Yokukansan and also some phytochemicals such as ω -6 PUFA and Gastrodin reduce the psychological symptoms in several ways in the patients undergoing operation. Most of the clinical studies were carried out on aromatherapy and the others were based on oral administration. Taken together, using medicinal herbs in medical settings before and after surgery is an effective alternative way for alleviating some psychological disorders such as anxiety, depression, aggressive and impulsive behavior, stress, delirium and cognitive dysfunction. However, the surgeons and anesthesiologists must be aware of their interaction and possible complications.

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Saeid Heidari-Soureshjani

✉ heidari_1983@yahoo.com**Introduction**

Surgical patients may undergo several psychological complications that can disturb the recovery trend and discharge from the hospital and

impose extra costs on them (1, 2). Psychological complications appear to be a significant and long-term which can cause prolonged recovery or long-lasting disability (3-6). Furthermore they have high frequency in surgery patients that lead to extra

morbidity and mortality (7). Patients awaiting surgery and postoperative patients who suffer from anxiety, stress, depression, delirium and other psychological disorders needs treatment and prophylaxis approaches for addressing and controlling these complications (1, 8). Alternative treatments consider as a widespread phenomenon prior to surgery (9). In this regard, use of medicinal plants in the treatment of diseases is one of the most popular methods because they are more safer than pharmaceutical drugs (10-14). Several studies have shown that medicinal herbs and their active ingredients, bioflavonoids, volatile oils and other substances can be effective, efficient and cheap for treatment against various disorders, such as psychological disorders (15-23).

Widespread use of medicinal herbs makes it important for surgeons and physicians to know about these drugs treatment effects and possible side effects in preoperative and postoperative patients (10, 24). Hence, medicinal plants are widely used before and after surgeries, all anaesthetists and surgeons must have to be familiarized with the potential perioperative complications of medicinal plants consumption (25). On the other hand, awareness of medical staff about their dedicated role is a vital issue in medical care (26-29). This review aims to investigate the effectiveness of medicinal herbs on psychological indices in patients undergoing surgery.

For doing this study, the keywords such as “anxiety”, “depression”, “aggressive”, “impulsive”, “stress”, “delirium” and “cognitive” in combination with “surgery” and medicinal plants search terms such as “medicinal plant” or “phyto” or “herb” were used to search for relevant publications indexed in the Institute for Scientific Information (ISI), Scopus and PubMed using EndNote software. A total of 1231 studies with mentioned keywords were added to the databank of the study (Supplementary Table 1).

A standard form, which included items such as author, the title or purpose of the study, intervention, variables, herbal dosage and outcome was designed. The full text of the articles that were in accordance with the purpose of the study were recorded in the form and entered into the study with the agreement of co-authors. Then, the studies that had positive effect on neonatal jaundice also were entered in the study. The articles where studies with non-positive effects, full texts that were not accessible, review articles, non-English or non Persian language articles, and studies that were not related to the aim of this study were excluded after all authors’ agreement was recovered. Finally, 36 articles were included in the study (Fig. 1).

Medicinal plants and their compounds can be effective on psychological disorders before and

after surgeries through various ways (Supplementary Table 2).

Medicinal plants and their derivatives reduce the psychological symptoms in several ways in the patients undergoing operation (Fig. 2). Most of the clinical studies were done on aromatherapy and the others were based on oral administration.

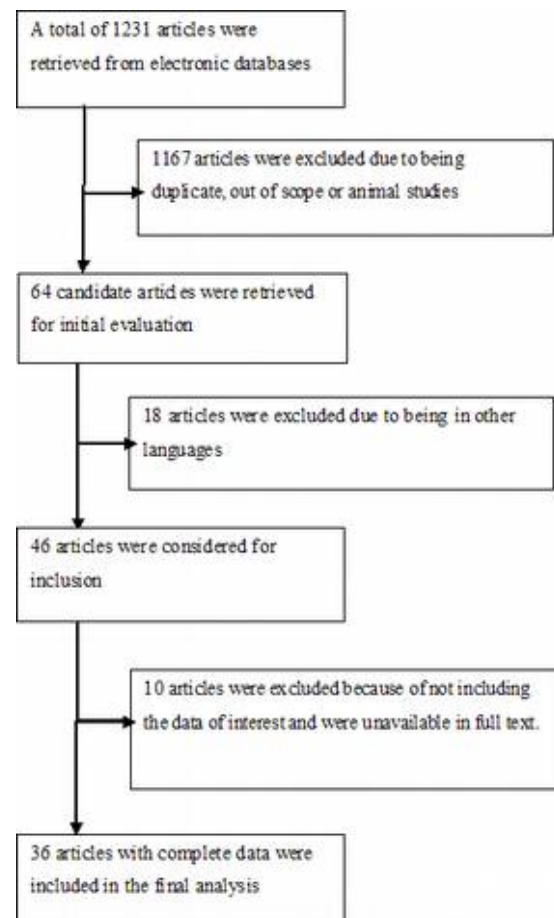


Fig. 1. Flowchart of the designed study

Aromatherapy

Many of the reviewed studies use the essential oil of the herbs as an aromatherapy method for their prophylactic effects against anxiety. Plants essential oils contain essence of the fragrance and that mainly contain two chemical groups which consist of terpenoids (sesquiterpenes and monoterpenes) and several phenylpropanoid derivatives (64, 65). On the other hand, essential oils and odor is composed of terpenes, alcohol, aldehydes, ethers, esters, ketones, oxides phenols and saturated and unsaturated hydrocarbons (66, 67). Essential oil in the medicinal herbs absorption occurs in lungs through respiration. They increase blood flow to the brain and able to cross the blood-brain barrier through respiration (66). Moreover, it is assumed that inhalation of the medicinal herbs’ fragrance can stimulate cell membranes of olfactory receptors (Ors) neurons which are responsible for the detection of odorants. This neurons transfer a message to the limbic system

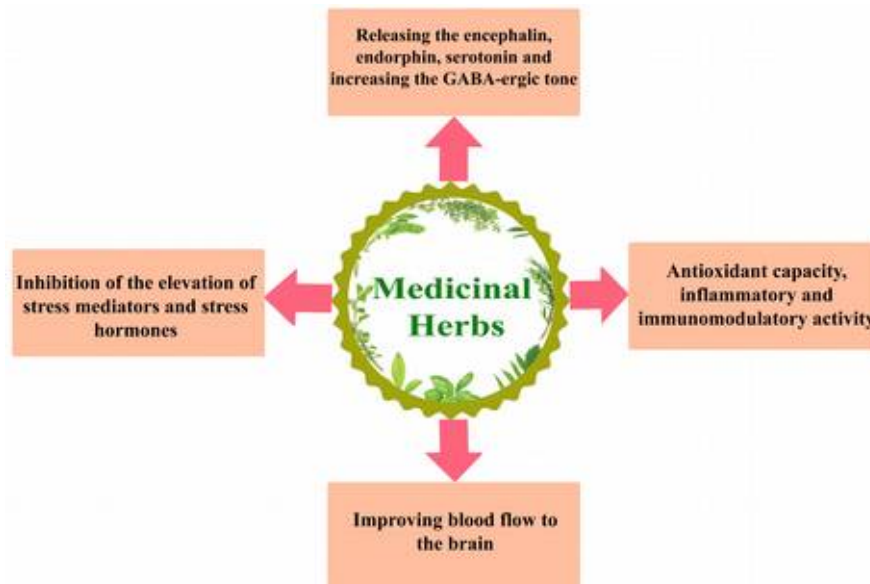


Fig. 2. Main mechanisms of the effects of medicinal herbs on psychological indices

(center of emotions) and the feeling center in the brain, release endorphin, enkephalin and serotonin. So mentioned neurotransmitters confront with stress and can bring calmness for the patients and reduce anxiety and depression (31, 68). Furthermore, essential oils can reduce pain, depression, anxiety, bipolar disorder and attention deficit hyperactivity disorder by activation of the γ -aminobutyric acid (GABA) receptor system (69). It should be noted that GABA is the chief inhibitory neurotransmitter in the vertebrate central nervous system and the GABA receptor system exerts a major inhibitory function in the brain. GABAergic system prevents us from generating inappropriate emotional and behavioral responses and its dysfunction has been implicated in several psychological disorders (70).

In this study, four study is reported that inhalation of medicinal plants oils cannot reduce psychological symptoms (39, 40, 49, 52). Maybe these inconsistencies may arise from ineffectiveness of short inhalation, diverse concentrations and due to different sample sizes. On the other hand, various illnesses may have different stress syndrome and experience varying degrees of anxiety. Therefore, this can interfere with study results. The clinical trials not reported any adverse side effects associated with aromatherapy and consider it as a safe method for reducing psychological symptom in pre and postoperative stages.

Oral administration

Clinical trials showed that edible consumption before and even after surgery, have prophylactic and therapeutic effects against stress, anxiety, delirium and cognitive disorders in patients. Some of the medicinal herbs, physiologically affect on stress in an indirect way by controlling inflammatory processes and stress mediators (53, 62). Some of them after intestinal absorption

entered the blood flow and like the aromatherapy can affect on brain neurotransmitters. They may play the role of agonistic and antagonistic agents on serotonin and dopamine receptors and can insert protective effects against the glutamate-induced excitatory neurotoxicity by amelioration of astrocyte dysfunction.

Although, in many reviewed clinical studies, positive outcomes were observed in controlling the psychological symptoms of patients, but in several studies, herbal treatments could not be effective in psychological disorders (47, 57, 58). Side effects and herb-drug interactions are the most important issue that anaesthetists and surgeons caution during oral administration. Cardiovascular instability, increased bleeding tendencies, hypertension, electrolyte disturbances, endocrine effects, coagulation disorders, renal failure and hepatotoxicity are attributed medicinal herbs side-effects in surgeries (25, 71-73). So, currently available data propose that unknown herbal treatments must be discontinued up to 2 weeks before and after elective surgery (61). No side effects were reported from oral intake of herbs in the reviewed clinical trials. But the important thing is that the most of the studies performed frequently on plants that had already been carried out on them. Therefore, this issue cannot provide a clear inference of medicinal herbs side effects in pre and postoperation periods.

Although most studies reported positive consequences in these disorders, there were some problems in designing studies. For example, the follow-up period was short in the studies and in some clinical studies blinding was not done or sample size was insufficient. Different samples with different severity of psychological problems as well as studies can affect the results. For instance, the patient who has a tumor removal surgery may affect major depression and this can

have impact on other psychological disorders (74) and may experience excessive stress than hernial surgery. So a herbal prescription cannot be of equal uses (time, dose) in both procedures. The other considerable thing is data collection method and outcome assessment. In the surveyed studies evaluation of psychological disorders has been relying on subjective assessment tools such as Depression Scale—Hospital Anxiety and Depression Scale (HADS-D), Spielbergers state anxiety inventory questionnaires, State-Trait Anxiety Inventory (STAI) and other instruments. In spite of this, if subjects fail to reliably report, subjective evaluation tools are not reliable (75, 76). However recently, measurement of biomarkers (and even concomitant with questionnaires) in some psychological disorders can non-invasively evaluate the patients' psychological status in more accurate way.

Conclusion

Use of medicinal herbs in medical settings before and after surgery is an effective alternative way for alleviating some psychological disorders such as anxiety, depression, aggressive and impulsive behavior, stress, delirium and cognitive dysfunction. But the surgeons and anaesthetists must be aware of their interaction and possible complications.

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Conflicts of interest

The authors declare no conflict of interest.

Authors contributions

All authors cooperated for writing the draft and they read and approved the manuscript.

References

1. Arruda APN, Ayala AP, Lopes LC, Bergamaschi CC, Guimaraes C, Grossi MD, et al. Herbal medications for surgical patients: a systematic review protocol. *BMJ Open* 2017; 7(7):e014290. <http://dx.doi.org/10.1136/bmjopen-2016-014290>
2. Alibeigi F, Hosseini M, Shabaniyan M, Shabaniyan A, Shabaniyan G. Comparison of hemodynamic changes, movement, duration of surgery and pain between lateral and supine position after spinal anesthesia in transurethral lithotripsy. *Journal of Renal Injury Prevention* 2019; 8(1):11-6. <http://dx.doi.org/10.15171/jrip.2019.03>
3. Pinto A, Faiz O, Davis R, Almoudaris A, Vincent C. Surgical complications and their impact on patients' psychosocial well-being: a systematic review and meta-analysis. *BMJ open* 2016; 6(2):e007224-e. <http://dx.doi.org/10.1136/bmjopen-2014-007224>
4. Akhlaghi M, Shabaniyan G, Rafieian-Kopaei M, Parvin N, Saadat M, Akhlaghi M. *Citrus aurantium* Blossom and Preoperative Anxiety. *Revista Brasileira de Anestesiologia* 2011; 61(6):702-12. [http://dx.doi.org/10.1016/S0034-7094\(11\)70079-4](http://dx.doi.org/10.1016/S0034-7094(11)70079-4)
5. Solati K. The efficacy of mindfulness-based cognitive therapy on resilience among the wives of patients with schizophrenia. *Journal of Clinical and Diagnostic Research* 2017; 11(4):VC01-VC3. <http://dx.doi.org/10.7860/JCDR/2017/23101.9514>
6. Haghayegh SA, Neshatdoost H, Drossman DA, Asgari K, Soulati SK, Adibi P. Psychometric characteristics of the Persian version of the irritable bowel syndrome quality of life questionnaire (P-IBS-QOL). *Pakistan Journal of Medical Sciences* 2012; 28(2):312-7.
7. Ghoneim MM, O'Hara MW. Depression and postoperative complications: an overview. *BMC surgery* 2016; 16:5. <http://dx.doi.org/10.1186/s12893-016-0120-y>
8. Prayson BE, Floden DP, Ferguson L, Kim KH, Jehi L, Busch RM. Effects of surgical side and site on psychological symptoms following epilepsy surgery in adults. *Epilepsy & Behavior* 2017; 68:108-14. <http://dx.doi.org/10.1016/j.yebeh.2016.11.004>
9. Wang SM, Peloquin C, Kain ZN. Attitudes of patients undergoing surgery toward alternative medical treatment. *Journal of Alternative and Complementary Medicine (New York, NY)* 2002; 8(3):351-6. <http://dx.doi.org/10.1089/10755530260128041>
10. Singh V, Mohammad S, Singh N. Herbs and surgery. *National Journal of Maxillofacial Surgery* 2012; 3(1):101-6. <http://dx.doi.org/10.4103/0975-5950.102180>
11. Asadi-Samani M, Rafieian-Kopaei M, Lorigooini Z, Shirzad H. A screening to determine total phenol and flavonoid content of some Iran's medicinal plants grown in chaharmahal va Bakhtyari province. *Indian Journal of Natural Products and Resources* 2018; 9(4):296-302.
12. Kooti W, Servatyari K, Behzadifar M, Asadi-Samani M, Sadeghi F, Nouri B, et al. Effective Medicinal Plant in Cancer Treatment, Part 2: Review Study. *Journal of Evidence-Based Complementary and Alternative Medicine* 2017; 22(4):982-95. <http://dx.doi.org/10.1177/2156587217696927>
13. Asadi-Samani M, Moradi MT, Mahmoodnia L, Alaei S, Asadi-Samani F, Luther T. Traditional uses of medicinal plants to prevent and treat diabetes; an updated review of ethnobotanical studies in Iran. *Journal of Nephropathology* 2017; 6(3):118-25. <http://dx.doi.org/10.15171/jnp.2017.20>
14. Kooti W, Hasanzadeh-Noohi Z, Sharafi-Ahvazi N, Asadi-Samani M, Ashtary-Larky D. Phytochemistry, pharmacology, and therapeutic uses of black seed (*Nigella sativa*). *Chinese Journal of Natural Medicines* 2016; 14(10):732-45. [http://dx.doi.org/10.1016/S1875-5364\(16\)30088-7](http://dx.doi.org/10.1016/S1875-5364(16)30088-7)
15. Heidari-Soreshjani S, Asadi-Samani M, Yang Q, Saeedi-Boroujeni A. Phytotherapy of nephrotoxicity-induced by cancer drugs: an updated review. *Journal of nephropathology* 2017; 6(3):254-63. <http://dx.doi.org/10.15171/jnp.2017.41>
16. Memarzadeh E, Luther T, Heidari-Soureshjani S. Effect and mechanisms of medicinal plants on dry eye disease: A systematic review. *Journal of Clinical and Diagnostic Research* 2018; 12(9):NE1-NE4.

17. Shabanian G, Heidari-Soureshjani S, Rafieian-Kopaei M, Saadat M, Shabanian M. Therapeutic effects of *Quercus persica* l fruit skin on healing of second-degree burn wounds in animal model. *Journal of Zanjan University of Medical Sciences and Health Services* 2017; 25(113):81-92.
18. Shabanian S, Khalili S, Lorigooini Z, Malekpour A, Heidari-Soureshjani S. The effect of vaginal cream containing ginger in users of clotrimazole vaginal cream on vaginal candidiasis. *Journal of Advanced Pharmaceutical Technology & Research* 2017; 8(2):80-4. http://dx.doi.org/10.4103/japtr.JAPTR_176_16
19. Shirani M, Raeisi R, Heidari-Soureshjani S, Asadi-Samani M, Luther T. A review for discovering hepatoprotective herbal drugs with least side effects on kidney. *Journal of Nephro Pharmacology* 2017; 6(2): 38-48. <http://dx.doi.org/10.15171/npj.2017.03>
20. Yavangi M, Rabiee S, Nazari S, Farimani-Sanoee M, Amiri I, Bahmanzadeh M, et al. Comparison of the effect of oestrogen plus *Foeniculum vulgare* seed and oestrogen alone on increase in endometrial thickness in infertile women. *Journal of Clinical and Diagnostic Research* 2018; 12(1):QC01-QC4. <http://dx.doi.org/10.7860/JCDR/2017/30164.11020>
21. Heidari-Soureshjani S, Asadi-Samani M, Yang Q, Saeedi-Boroujeni A. Phytotherapy of nephrotoxicity-induced by cancer drugs: An updated review. *Journal of Nephropathology* 2017; 6(3):254-63. <http://dx.doi.org/10.15171/jnp.2017.41>
22. Shirani-Boroujeni M, Heidari-Soureshjani S, Keivani Hafshejani Z. Impact of oral capsule of *Peganum harmala* on alleviating urinary symptoms in men with benign prostatic hyperplasia; a randomized clinical trial. *Journal of renal injury prevention* 2017; 6(2):127-31. <http://dx.doi.org/10.15171/jrip.2017.25>
23. Khosravian P, Heidari-Soureshjani S, Yang Q. Effects of medicinal plants on radiolabeling and biodistribution of diagnostic radiopharmaceuticals: A systematic review. *Plant Science Today* 2019; 6(2):123-31. <http://dx.doi.org/10.14719/pst.2019.6.2.513>
24. Shabanian G, Shabanian M, Shabanian A, Heidari-Soureshjani S. Comparison of atracurium and methocarbamol for preventing succinylcholine-induced muscle fasciculation: A randomized controlled trial. *Journal of Advanced Pharmaceutical Technology and Research* 2017; 8(2):59-62. http://dx.doi.org/10.4103/japtr.JAPTR_172_16
25. Wong A, Townley SA. Herbal medicines and anaesthesia. *BJA Education*. 2010; 11(1):14-7.
26. Yazici G, Erdogan Z, Bulut H, Ay A, Kalkan N, Atasayar S, et al. The use of complementary and alternative medicines among surgical patients: A survey study. *Journal of Perianesthesia Nursing* 2019; 34(2):322-9. <http://dx.doi.org/10.1016/j.jopan.2018.04.007>
27. Yilmaz F, Çifci HE. Herbal use among presurgical patients in turkey: A cross-sectional study. *Anesthesiology Research and Practice* 2018; 2018:5. <http://dx.doi.org/10.1155/2018/1643607>
28. Hasanpour-Dehkordi A, Dehghani A, Solati K. A comparison of the effects of pilates and mckenzie training on pain and general health in men with chronic low back pain: A randomized trial. *Indian Journal of Palliative Care* 2017; 23(1):36-40. <http://dx.doi.org/10.4103/0973-1075.197945>
29. Afkhami-Ardakani M, Hassanzadeh S, Shahrooz R, Asadi-Samani M, Latifi M, Luther T. Phytotherapy and phytopharmacology for reduction of cyclophosphamide-induced toxicity in the male urinary system. *Journal of Renal Injury Prevention* 2017; 6(3):164-70. <http://dx.doi.org/10.15171/jrip.2017.32>
30. Fayazi S, Babashahi M, Rezaei M. The effect of inhalation aromatherapy on anxiety level of the patients in preoperative period. *Iranian Journal of Nursing and Midwifery Research* 2011; 16(4):278-83.
31. Bakhsha F, Mazandarani M, Aryaei M, Jafari SY, Bayate H. Phytochemical and anti-oxidant activity of *Lavandula angustifolia* mill. Essential oil on preoperative anxiety in patients undergoing diagnostic curettage. *International Journal of Women's Health and Reproduction Sciences* 2014; 2(4):268-71.
32. Franco L, Blanck TJJ, Dugan K, Kline R, Shanmugam G, Galotti A, et al. Both lavender fleur oil and unscented oil aromatherapy reduce preoperative anxiety in breast surgery patients: a randomized trial. *Journal of Clinical Anesthesia* 2016; 33:243-9. <http://dx.doi.org/10.1016/j.jclinane.2016.02.032>
33. Karaman T, Karaman S, Dogru S, Tapar H, Sahin A, Surem M, et al. Evaluating the efficacy of lavender aromatherapy on peripheral venous cannulation pain and anxiety: A prospective, randomized study. *Complementary Therapies in Clinical Practice* 2016; 23:64-8. <http://dx.doi.org/10.1016/j.ctcp.2016.03.008>
34. Hasanzadeh F, Kashouk NM, Amini S, Asili J, Emami SA, Vashani HB, et al. The effect of cold application and lavender oil inhalation in cardiac surgery patients undergoing chest tube removal. *EXCLI Journal* 2016; 15:64-74. <http://dx.doi.org/10.17179/excli2015-748>
35. Beyliklioglu A, Arslan S. Effect of lavender oil on the anxiety of patients before breast surgery. *Journal of Perianesthesia Nursing* 2019; 34(3):587-593. <http://dx.doi.org/10.1016/j.jopan.2018.10.002>
36. Jaruzel CB, Gregoski M, Mueller M, Faircloth A, Kelechi T. Aromatherapy for preoperative anxiety: A pilot study. *Journal of Perianesthesia Nursing* 2019; 34(2):259-64. <http://dx.doi.org/10.1016/j.jopan.2018.05.007>
37. Fenko A, Loock C. The influence of ambient scent and music on patients' anxiety in a waiting room of a plastic surgeon. *Health Environments Research and Design Journal* 2014; 7(3):38-59.
38. Wotman M, Levinger J, Leung L, Kallush A, Mauer E, Kacker A. The efficacy of lavender aromatherapy in reducing preoperative anxiety in ambulatory surgery patients undergoing procedures in general otolaryngology. *Laryngoscope Investigative Otolaryngology* 2017; 2(6):437-41. <http://dx.doi.org/10.1002/lio2.121>
39. Ayik C, Ozden D. The effects of preoperative aromatherapy massage on anxiety and sleep quality of colorectal surgery patients: A randomized controlled study. *Complementary Therapies in Medicine* 2018; 36:93-9. <http://dx.doi.org/10.1016/j.ctim.2017.12.002>
40. Bikmoradi A, Seifi Z, Poorolajal J, Aragchian M, Safiaryan R, Oshvandi K. Effect of inhalation aromatherapy with lavender essential oil on stress and vital signs in patients undergoing coronary artery bypass surgery: A single-blinded randomized clinical trial. *Complementary Therapies in Medicine* 2015; 23(3):331-8. <http://dx.doi.org/10.1016/j.ctim.2014.12.001>
41. Aslanargun P, Aslan E, Cuvaz O, Yuksel MU, Dikmen B. *Passiflora incarnata* Linneaus as an anxiolytic before spinal anesthesia. *Journal of Anesthesia* 2012; 26(1):39-44. <http://dx.doi.org/10.1007/s00540-011-1265-6>
42. Pinheiro MLP, Alcântara CEP, De Moraes M, De Andrade ED. *Valeriana officinalis* L. for conscious sedation of patients submitted to impacted lower third molar

- surgery: A randomized, double-blind, placebo-controlled split-mouth study. *Journal of Pharmacy and Bioallied Sciences* 2014; 6(2):109-14. <http://dx.doi.org/10.4103/0975-7406.129176>
43. Hassani S, Alipour A, Darvishi Khezri H, Firouzian A, Emami Zeydi A, Gholipour Baradari A, et al. Can *Valeriana officinalis* root extract prevent early postoperative cognitive dysfunction after CABG surgery? A randomized, double-blind, placebo-controlled trial. *Psychopharmacology* 2015; 232(5):843-50. <http://dx.doi.org/10.1007/s00213-014-3716-x>
 44. Rokhtabnak F, Ghodratty MR, Kholdebarin A, Khatibi A, Seyed Alizadeh SS, Koleini ZS, et al. Comparing the effect of preoperative administration of melatonin and *Passiflora incarnata* on postoperative cognitive disorders in adult patients undergoing elective surgery. *Anesthesiology and Pain Medicine* 2016; 7(1):e41238-e. <http://dx.doi.org/10.5812/aapm.41238>
 45. Dantas LP, de Oliveira-Ribeiro A, de Almeida-Souza LM, Groppo FC. Effects of *Passiflora incarnata* and midazolam for control of anxiety in patients undergoing dental extraction. *Medicina Oral Patologia Oral y Cirugia Bucal* 2017; 22(1):e95-e101. <http://dx.doi.org/10.4317/medoral.21140>
 46. Dehghan K, Kalani Z. Comparison of the effect of *Citrus aurantium* and oxazepam on the preoperative anxiety of patients candidate for coronary artery implantation operation. *Journal of Research in Medical and Dental Science* 2018; 6(2):1-5.
 47. Moazen-Zadeh E, Abbasi SH, Safi-Aghdam H, Shahmansouri N, Arjmandi-Beglar A, Talasaz A, et al. Effects of saffron on cognition, anxiety, and depression in patients undergoing coronary artery bypass grafting: A randomized double-blind placebo-controlled trial. *Journal of Alternative and Complementary Medicine* 2018; 24(4):361-8. <http://dx.doi.org/10.1089/acm.2017.0173>
 48. Soltanpour A, Alijaniha F, Naseri M, Kazemnejad A, Heidari MR. Effects of *Melissa officinalis* on anxiety and sleep quality in patients undergoing coronary artery bypass surgery: A double-blind randomized placebo controlled trial. *European Journal of Integrative Medicine* 2019; 28:27-32. <http://dx.doi.org/10.1016/j.eujim.2019.01.010>
 49. de Jong M, Lucas C, Bredero H, van Adrichem L, Tibboel D, van Dijk M. Does postoperative 'M' technique@massage with or without mandarin oil reduce infants' distress after major craniofacial surgery? *Journal of Advanced Nursing* 2012; 68(8):1748-57. <http://dx.doi.org/10.1111/j.1365-2648.2011.05861.x>
 50. Amini R, Alizadeh F. Investigating musical effects and aromatherapy on anxiety and pain in patients undergoing surgery. *Indian Journal of Forensic Medicine and Toxicology* 2018; 12(4):170-6. <http://dx.doi.org/10.5958/0973-9130.2018.00219.0>
 51. Dagli R, Avcu M, Metin M, Kiymaz S, Ciftci H. The effects of aromatherapy using rose oil (*Rosa damascena* Mill.) on preoperative anxiety: A prospective randomized clinical trial. *European Journal of Integrative Medicine* 2019; 26:37-42. <http://dx.doi.org/10.1016/j.eujim.2019.01.006>
 52. Fazlollahpour-Rokni F, Shorofi SA, Mousavinasab N, Ghafari R, Esmaeili R. The effect of inhalation aromatherapy with rose essential oil on the anxiety of patients undergoing coronary artery bypass graft surgery. *Complementary Therapies in Clinical Practice* 2019; 34:201-7. <http://dx.doi.org/10.1016/j.ctcp.2018.11.014>
 53. Kimura M, Sasada T, Kanai M, Kawai Y, Yoshida Y, Hayashi E, et al. Preventive effect of a traditional herbal medicine, Hochu-ekki-to, on immunosuppression induced by surgical stress. *Surgery Today* 2008; 38(4):316-22. <http://dx.doi.org/10.1007/s00595-007-3631-4>
 54. Saito S, Kobayashi T, Osawa T, Kato S. Effectiveness of Japanese herbal medicine yokukansan for alleviating psychiatric symptoms after traumatic brain injury. *Psychogeriatrics* 2010; 10(1):45-8. <http://dx.doi.org/10.1111/j.1479-8301.2010.00313.x>
 55. Arai YC, Kawanishi J, Sakakima Y, Sueoka S, Ito A, Tawada Y, et al. The effect of the Kampo medicine Yokukansan on preoperative anxiety and sedation levels. *Evid-Based Compl Alt.* 2014; 2014. <http://dx.doi.org/10.1155/2014/965045>
 56. Kamiya M, Aoyama T, Sugano N, Sato T, Yamamoto N, Taguri M, et al. Randomized phase II study of TJ-54 (Yokukansan) for postoperative delirium in gastrointestinal malignancy patients. *Journal of Clinical Oncology* 2017; 35(4 suppl):115. http://dx.doi.org/10.1200/JCO.2017.35.4_suppl.115
 57. Mizuno S, Takeuchi S, Kishiwada M, Mizutani N, Matsuda M, Sekoguchi N, et al. Incidence and risk factors of postoperative delirium following pancreatic surgery: does the administration of tj-54 reduce the incidence of delirium. *Digestive Surgery* 2018; 35(1):1-10. <http://dx.doi.org/10.1159/000456627>
 58. Morita J, Aoyama T, Sugano N, Sato T, Amano S, Nagashima T, et al. 515PRandomized phase II study of TJ-54 (Yokukansan) for postoperative delirium in gastrointestinal and lung malignancy patients. *Annals of Oncology* 2017; 28(suppl_10). <http://dx.doi.org/10.1093/annonc/mdx676.014>
 59. Sugano N, Aoyama T, Sato T, Kamiya M, Amano S, Yamamoto N, et al. Randomized phase II study of TJ-54 (Yokukansan) for postoperative delirium in gastrointestinal and lung malignancy patients. *Molecular and Clinical Oncology* 2017; 7(4):569-73. <http://dx.doi.org/10.3892/mco.2017.1357>
 60. Wada S, Inoguchi H, Hirayama T, Matsuoka YJ, Uchitomi Y, Ochiai H, et al. Yokukansan for the treatment of preoperative anxiety and postoperative delirium in colorectal cancer patients: a retrospective study. *Japanese Journal of Clinical Oncology* 2017; 47(9):844-8. <http://dx.doi.org/10.1093/jjco/hyx080>
 61. Wada S, Sadahiro R, Matsuoka YJ, Uchitomi Y, Yamaguchi T, Shimizu K. Yokukansan for preoperative psychiatric symptoms in cancer patients undergoing high invasive surgery. J-SUPPORT 1605 (ProD Study): study protocol for a randomized controlled trial. *Trials* 2019; 20(1):110. <http://dx.doi.org/10.1186/s13063-019-3202-1>
 62. Furukawa K, Yamamori H, Takagi K, Hayashi N, Suzuki R, Nakajima N, et al. Influences of soybean oil emulsion on stress response and cell-mediated immune function in moderately or severely stressed patients. *Nutrition* 2002; 18(3):235-40.
 63. Zhang Z, Ma P, Xu YN, Zhan MJ, Zhang YJ, Yao SL, et al. Preventive effect of gastrodin on cognitive decline after cardiac surgery with cardiopulmonary bypass: A double-blind, randomized controlled study. *Journal of Huazhong University of Science and Technology-Medical Sciences* 2011; 31(1):120-7. <http://dx.doi.org/10.1007/s11596-011-0162-4>
 64. Regnault-Roger C, Vincent C, Arnason JT. Essential oils in insect control: low-risk products in a high-stakes world. *Annual Review of Entomology* 2012; 57:405-24. <http://dx.doi.org/10.1146/annurev-ento-120710-100554>
 65. Tankam JM, Ito M. Inhalation of the essential oil of *Piper guineense* from Cameroon shows sedative and

- anxiolytic-like effects in mice. *Biological and Pharmaceutical Bulletin* 2013; 36(10):1608-14.
66. Ali B, Al-Wabel NA, Shams S, Ahamad A, Khan SA, Anwar F. Essential oils used in aromatherapy: A systemic review. *Asian Pacific Journal of Tropical Biomedicine* 2015; 5(8):601-11. <http://dx.doi.org/10.1016/j.apjtb.2015.05.007>
67. Wildwood C. *The encyclopedia of aromatherapy*: Healing Arts Press Rochester, VT; 1996.
68. Wang Z-J, Heinbockel T. Essential oils and their constituents targeting the gabaergic system and sodium channels as treatment of neurological diseases. *Molecules* (Basel, Switzerland) 2018; 23(5):1061. <http://dx.doi.org/10.3390/molecules23051061>
69. Lee YL, Wu Y, Tsang HW, Leung AY, Cheung WM. A systematic review on the anxiolytic effects of aromatherapy in people with anxiety symptoms. *J Altern Complement Med.* 2011; 17(2):101-8. <http://dx.doi.org/10.1089/acm.2009.0277>
70. Semyanov A, Walker MC, Kullmann DM, Silver RA. Tonically active GABA A receptors: modulating gain and maintaining the tone. *Trends in Neurosciences* 2004; 27(5):262-9. <http://dx.doi.org/10.1016/j.tins.2004.03.005>
71. Kleinschmidt S, Rump G, Kotter J. Herbal medications. Possible importance for anaesthesia and intensive care medicine. *Der Anaesthesist* 2007; 56(12):1257-66. <http://dx.doi.org/10.1007/s00101-007-1264-z>
72. Batra YK, Rajeev S. Effect of common herbal medicines on patients undergoing anaesthesia. *Indian Journal of Anaesthesia* 2007; 51(3):184-192.
73. Hodges PJ, Kam P. The peri-operative implications of herbal medicines. *Anaesthesia* 2002; 57(9):889-99. <http://dx.doi.org/10.1046/j.1365-2044.2002.02781.x>
74. İzci F, İlgün AS, Fındıklı E, Özmen V. Psychiatric symptoms and psychosocial problems in patients with breast cancer. *The Journal of Breast Health* 2016; 12(3):94-101. <http://dx.doi.org/10.5152/tjbh.2016.3041>
75. Yamaguchi M, Deguchi M, Wakasugi J, Ono S, Takai N, Higashi T, et al. Hand-held monitor of sympathetic nervous system using salivary amylase activity and its validation by driver fatigue assessment. *Biosensors and Bioelectronics* 2006; 21(7):1007-14. <http://dx.doi.org/10.1016/j.bios.2005.03.014>
76. ARAI YC, Sakakibara S, Ito A, Ohshima K, Sakakibara T, Nishi T, et al. Intra-operative natural sound decreases salivary amylase activity of patients undergoing inguinal hernia repair under epidural anesthesia. *Acta Anaesthesiologica Scandinavica* 2008; 52(7):987-90. <http://dx.doi.org/10.1111/j.1399-6576.2008.01649.x>

