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PRINCIPLES OF ESSENTIAL OILS USING FOR MEDICAL PURPOSES. A REVIEW

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Introduction

Empirical experience of essential oils successful application as medicines has been confirmed with the latest research methods.

Range of beneficial effects of essential oils (EO) on living organisms is so wide that it is difficult to name the area of medicine or a disease in which application of EO has not been researched on, so literary references cited in the article, should be considered only as the examples of EO particular effects.

The purpose of the review is to inform practitioners about the rules that should be followed when working with EO and possible side effects.

General information about essential oils

Currently, there are about 3000 names of essential oils. Approximately 300 EO are widely used in medical and veterinary practice, food and cosmetic industry and as a part of household chemicals [46]. Essential oils are oily liquids from light yellow to brown, almost insoluble in water (0.05 %), but well-volatile even at room temperature, as a rule, have a pleasant odor. EO are active against bacteria, mycoplasma, fungi, viruses, protozoa and parasites, have anti-inflammatory, antioxidant, antimutagenic properties. It has been shown that they slow down the aging process, activate regeneration processes in organs and tissues, activate the immune system, prevent development of malignant tumors [21], reduce the toxic effects of xenobiotics [13], ionizing radiation [3] and optimize the performance of systems and tissues, exhibiting the properties of adaptogens and improving quality of life [11].

However, using the EO, it should be remembered that they are complex chemical mixtures which are highly dependent on climate zone where the raw material was grown, harvest season, weather conditions and other factors [38]. Composition and dose of the oil determine severity and direction of its pharmacological effects [23].

It should be also noted that the effect of using any EO for humans will largely depend on sex, age, type of the human nervous system and its state (agitation, fatigue, a state of rest) at the time of aromatherapy.

Standardization of essential oils

Only natural essential oils that are appropriate to the international standards on the content of the main components are recommended to use for aromatherapy [28].

In the composition of essential oils 50-500 or more components could be found, that depends only on the sensitivity of the apparatus. Information about EO composition could be found at the site by Vinogradov B.A. [2]. As an example Table. 1 demonstrates the results of chromatographic analysis of peppermint EO components from Ukrainian raw materials.

Table 1

The result of chromatographic analysis of peppermint EO from Ukrainian raw materials

№	Component	%	№	Component	%
2	α - pinen	0.55	23	carvone	.04
3	sabinene	0.23		piperitone	.01
4	β - pinen	0.64	26	linalyl acetate	.14
5	myrcene	0.27	28	neomenthyl acetate	.09
6	p-cymene	0.07	29	menthyl acetate	.35
7	1,8-cineole	0.51	30	thymol	.04
8	limonene	3.42	31	isomenthyl acetate	.21
9	trans-cymene	0.05	32	α -cubebene	.05
10	nonanal	0.07	33	β -bourbonen	.25
11	linalool	0.14	34	β -elemene	.08
12	amyl isovalerate	0.08	35	α -gurjunene	.14
13	3-octyl acetate	0.03	36	caryophyllene	.67
14	methone	14.4	37	gumulene	.09
15	citronellal	0.05	38	β - farnesene	.17
16	isomethone	2.25	39	germacrene D	.64
17	menthofuran	0.29	40	γ - elemene	.13
18	neomenthol	2.97	41	α -farnesene	.05
19	menthol	58.7	42	δ -cadenene	.08
20	isomenthol	0.84	43	spathulenol	.06
21	α -terpineol	0.15	44	aryophyllenox	.21
22	pulegone	0.26	45	viridiflorol	.11

The table shows that menthol, its isomers and derivatives are $\approx 84\%$ in peppermint oil, 3 more substance (piperitone, caryophyllene and limonene) are from 1 to 3.5% (of $\approx 7\%$), while the remaining 34 components are represented by tenths and hundredths of a percent.

In other mint varieties component composition may vary considerably, but the main components of peppermint oil will be menthol and its derivatives.

Expensive EO are often faked by diluting them with cheaper ones, vegetable oils or synthetic substitutes, which have a similar smell, but do not have the pharmacological properties of essential oils natural components could be sold instead of them.

When buying EO it's better to obtain quality certificate and address of the manufacturer. It is not excluded, however, that adulterated oil will be accompanied by the relevant documents.

Studies of EO samples from different climatic zones showed significant differences in their chemical composition and pharmacological properties. Studies of EO from plants grown in the field in Finland, where a short period of plant growth (2-3 months) is largely offset by a long daylight in summer - 19 hours and more, a lower content of major phenolic components than in their southern analogues was found. So, carvacrol - one of the main components of

Thymus oil, was not found in Finnish sample [38]. For comparison, in EO from Crimean varieties of *Thymus carvacrol* part was from 16% to 72% in carvacrol varieties [7].

EO samples of sage leaves harvested in different seasons, also differed in composition: oil from the raw material collected in January, contained more camphor (12.3%), thujone (1.9%) and camphene (4.8%) was more toxic while intraperitoneal injection in mice (LD50 = 839 mg / kg) and had higher convulsive action. It has been found high degree correlation between these components content and toxicity: spring feedstock oil contained less camphor (7.7%), thujone (1.3%), camphene (3.1%) and was less toxic (LD50 = 1200 mg / kg). Therefore we recommend using of oil from spring raw material for medical purposes [23].

Thus composition and pharmacological properties of the essential oils from the same plant species, varies within wide limits and depend on the genotype, stage of plant maturity, climate, place of growth and other factors [16, 36, 38, 40, 44].

Standardization of EO is carried out by number of the main components, as therapeutic effect may depend on the interaction of several minor components. Sometimes under the influence of minor components toxicity of the main components reduced.

Thus among all possible options the most reliable way is purchasing oils from the same reliable manufacturer – this is the only way to work with the product with already known effect.

EO storage and expiration date

In the public literature, which is uncritically replicated and further cited including the Internet, one can find, for example, such statements: "Terms of use for essential oils are not limited. Moreover, the "thin" oils such as verbena, rose, neroli, sage, as well as "thin" wines are refined during prolonged storage "[10] – it is a completely wrong statement.

After 3 years of storage at + 8-10 °C in glass jars chemical composition of lavender, mint and *Monarda* EO changed within the permissible standards. Absolute rose and jasmine oxidized so that it could be determined even organoleptically.

All EO oxidize and decompose in air and light: changing color, odor, viscosity, acid number increases, resins isomers and derivatives of original substances form in oils:

- some components of EO of *Atractylodes* (*Atractylodes macrocephalae* Pall.) self oxidized during the first hours, even at room temperature [26]. After six months of storage in the oil from *Atractylodes* root amount of the main components - β -celine, hinesol, β -eudesmol and α -bisabolol reduced significantly [20];

- when stored for 3 months at 37°C in EO of Sichuan lovage root (*Ligusticum chuanxiong* Hort.) the amount of the main component - ligustilide reduced, the amount of 2-propylene-1-hexane increased and isomers that were not present in the fresh oil appeared [15].

In the open air and on contact with oxidants limonene, linalyl acetate and geraniol are oxidized forming peroxides, aldehydes, alcohols and ketones, which already have high allergenic properties (influence of oxidation products is described below).

Therefore, EO should only be stored in a dark glass jars with glass or cork plugs, without air. Long-term contact with EO breaks even polyethylene structure and most rubbers destroy and pollute EO with decay products.

In practice, it is necessary to have the vial with EO for long term storage and mold the oil into the working tank when necessary. One should not buy EO in amount greater than needed for 2-3 years of work.

Terms of use for EO mixtures are less than for single ones. Terms of use for mixtures of EO with fatty oils and diluents progressively reduced and their pharmacological effects of varies unpredictably.

Currently it is published hundreds of the recipes for mixtures of several essential oils that are recommended as aphrodisiacs, compositions for "rejuvenation", "weight loss" and so on. Compositions which include up to 40 types of extracts and essential oils are patented. Most of these compositions are the advertising production without scientific confirmation of their useful properties, safety, and allowable storage time. The authors of most of these compositions are people who speculate on the interests of a particular group of customers.

Precautions when working with essential oils

Essential oils are very active pharmacological substances, so before using them all patients should be olfactory or patch testing: a person is given a sniff test probe with EO or it's making a smear on the skin of the inner surface of the forearm with diluted EO. Patients were followed for at least 30 minutes (longer if possible) and poll the next day. Complaints of sore throat, sneezing, coughing, difficulty breathing, changes in blood pressure and heart rate, itching and irritation of the skin - the emergence of such symptoms on the test day or later should be considered a contraindication to the use of EO to the patient.

Oils should be applied to the skin in a diluted form - in a cream or fatty oils: hazelnut, almond, jojoba, sesame, apricot. The exceptions are the acupuncture points where 1-2 drops of whole oil are applied.

EO should be recommended with great care for elderly people, children under one year and pregnant women.

Cases of skin irritation often associated with the use of old, oxidized oils. Due to prolonged contact with EO massage therapists often have hypersensitivity, contact dermatitis, and intolerance to some EO. Recurrence of skin symptoms after drinking lemongrass tea has been described. The authors consider it is necessary to inform workers that have prolonged contact with essential oils about the possibility of increasing sensitivity to these substances and risk of further limiting their ability to continue work in this sphere [17].

Of course, care should be taken that the oils do not fall on the conjunctiva of the eye.

Contra-indications for EO use

In the literature there are warnings about use of EO when certain diseases and syndromes are noticed:

- EO of basil and cypress increase blood clotting. This should be considered when assigning patients with thrombophlebitis, not to assign these oils for people with stroke and heart attack.
- EO of juniper, fir and sandalwood are contraindicated in nephritis.
- EO of bergamot, ylang-ylang, lemon, neroli, grapefruit, petit-Grein and orange have photosensitizing effect (increase skin sensitivity to UV rays). Photosensitization and other

negative effects after application of bergamot oil have been noted by many researchers [25, 30, 55, 56].

Special attention should be given to the review of articles about lavender, prepared by the Research Foundation of National USA Standards in 1994-2006. The authors concluded that there was insufficient level of scientific evidence on the safety of lavender essential oil use in medicine, particularly combined with other drugs:

- So, lavender enhances the effect of barbiturates (phenobarbital), tranquilizers and muscle relaxants, (lorazepam and diazepam), narcotics (codeine), certain antidepressants (imipramine), alcohol and substances that reduce cholesterol.

- When used with anticoagulants (aspirin, heparin, and warfarin) or NSAIDs (ibuprofen, naproxen) lavender EO can enhance bleeding.

- Provides information about the possibility of other side effects - allergies, dermatitis and others.

The authors considered there is no sufficient evidence of safety and feasibility of using lavender oil for children and adolescents younger than 18 years. The article is highly recommended to use lavender drugs only after consultation with experienced professionals [52].

If one of the most studied EO, used in medicine for hundreds of years in different countries, found so many accessory effects, probably, exotic oils should be used with caution, as information about them is often limited only by their use in ethnomedicine.

In early pregnancy it does not recommend to use EO in general, especially EO of basil, verbena, cloves, oregano, hyssop, cedar, cypress, myrrh, juniper, patchouli, rosemary, yarrow, thyme and sage [22].

For patients with hypertension, epilepsy, neurological disorders, and kidney disease treatments with oils of black pepper, rosemary and sage are contraindicated [45].

The official medicine in Russia allows medication of essential oils only in diluted form and only in official medicines. The Register of Medicinal Products includes about 40 products of native production, containing essential oils and their components [13] in combinations that allow to use the lowest effective dose of each of them and to reduce the possibility of accessory effects that occur when using high doses of essential oils.

Most products contain in its composition essential oils of mint and eucalyptus; lavender, clove, Ahearn, fir, pine and turpentine oils are used rarely. Pharmacological effects of the essential oils is enhanced by addition to the preparations of terpenoids such as menthol, thymol and camphor or alcoholic extracts and infusions of chamomile, thyme, yarrow, oregano and hops. Mostly these are medicines of antiseptic, anti-inflammatory and wound-healing activity for treatment of respiratory and gastrointestinal tracts and kidney diseases, infected wounds and burns [6].

The composition of foreign drugs except eucalyptus and peppermint can include EO of rosemary, rose, cinnamon, thyme, lemon balm oil and others [4].

Toxicity of essential oils

Some authors consider plants containing EO as sources of potentially toxic substances [24].

Indeed, the toxic effect of vapor terpene compounds was found for workers of aromatic plants industries: under prolonged exposure of menthol and coriander oil vapors at the concentrations of 50-100 mg / m³ signs of chronic poisoning in the form of changes in the kidney, liver, lung tissue [33], pathology of gastrointestinal tract and cardiovascular system [8, 9] were observed. When collecting aromatic raw materials, some workers complained of headache, nausea, vomiting, conjunctivitis, itching and rashes on the skin [14].

EO of cloves has long been used in medicine, cosmetics and it is considered safe. However, adding 0.03% clove EO and 0.25% lavender EO *in vitro* cytotoxic effect of linalyl acetate and essential oils over the culture of human skin cells was detected. Toxicity of linalyl acetate was even higher than that of whole lavender oil; obviously its toxic effect was inhibited in the whole oil with other components [39].

For lavender EO cytotoxicity properties were described in relation to skin cells [27, 39, 41], and tea tree, mandarin, benzoin and ylang-ylang EO can cause allergic reactions when applied to skin [17, 19, 34, 35, 43, 47, 54, 55]. Allergic reactions are described in contact with the particular components of essential oils - benzyl and cinnamyl alcohols, eugenol, geraniol, hydroxycitronellal and others.

Linalool (3,7-dimethyl-1,6-octadiene-3-ol) presented in large quantities in many EO has a fresh floral scent and is therefore often used as a flavoring in the goods of household chemicals and cosmetics. In its pure form linalool is very weak allergen and does not cause skin irritation. In the air or on contact with oxidants linalool oxidized and forms substances with allergenic properties.

In this model, simulating linalool storage conditions, it was subjected to air oxidation. After 45 weeks storage mixture had only 30% of linalool. Furthermore the mixture contains 19% of linalool hydroperoxides (including 15% of 7-hydroperoxy-3,7-dimethylocta-1,5-dien-3-ol, 4% 6-hydroperoxy-3,7-dimethylocta-1,7-dien-3-ol, 20% of 2-(5-methyl-5-viniltetragidrofuran-2-yl) propan-2-ol, 4% of 2,2,6-trimethyl-6-2-viniltetragidropiren-3-ol), and others. Sensitizing properties were characteristic mostly for hydroperoxides; esters did not exhibit such properties.

The authors supposed that contact allergy to linalool is more common than previously thought. Thus, patients suffering from skin dermatitis in 5-7% of cases demonstrated positive reaction to linalool. Such a high frequency of positive reactions places linalool among the most common contact allergens [18, 31, 37, 42, 48, 49, 50, 51].

EO toxic components are α - and β -thujone, ledol, cymene, palyustrol and arbutin. International Society for Polycyclic Aromatic Compounds prohibited for use in aromatherapy EO of tansy, wild rosemary, Cinnamomum, rue, saffron and arborvitae [29], for which it has been described the possibility of toxic effects on the central nervous system, liver and excretory system [20].

Effective concentration of essential oils

Indications and recommended doses of essential oils can greatly vary from different authors. Therefore, review of the literature should be critical in the part of the recommendations on EO use.

During the aromatherapy session patients inhale vaporized EO in the concentration 1-3 mg / m³ of air. At relaxed state, in the sitting position a person inhales 5-8 l / min. of the air. Simple arithmetic calculation shows that during aromatherapy session of 20-30 minutes the patient breathes 0.1-0.2 m³ of the air ie \approx 0.1-0.6 mg of EO [13].

Doses in tenth parts of a milligram, has a significant impact on health, heart rate, blood pressure, memory, attention, physical performance, regeneration processes, immune system, etc.

Keep this in mind when assigning other procedures with EO - baths, massage, treatment of wounds and burns.

Some authors recommend using of undiluted EO for the massage, and it is at least 5 ml per procedure. We think that recommendations of aromatherapists who advise to dilute EO and use much smaller amounts have better foundation. Thus, Brown [1] recommended 3 drops of EO per 10 ml of neutral oils for massage and 2-3 drops of EO three times a day not

more than three weeks for ingestion. The author believes that in large doses essential oils are harmful and dangerous.

From our point of view, the ingestion of 6-9 drops of oil (50-300mg) per day is too much. Drops dosage itself is a very conditional and imprecise method, since the weight of a drop depends on the viscosity of the oil and application tools. When weighing on analytical scales lavender oil drop from the glass pipette was 30-35mg, and a drop of the same oil from syringe with intradermal needle - 5-7 mg.

EO successfully used for the treatment of infected wounds and superficial skin lesions of different nature. We have observed the acceleration of engraftment after skin plasty, acceleration of epithelialization of the wound edges, the appearance of islands of epithelium on the wound surface and reducing scar formation [14]. In the treatment of wounds, ulcers` abrasions and other skin lesions 5-7 times diluted EO should be used [32].

It is also recommended to add not more than 3-5 drops of EO in the bath; the addition of saponificative substances under this amount of oil is not required.

Dose-dependence of various beneficial effects of EO was noted by most of authors. Schematically, this is reduced to the usual sequence: lack of low concentrations effect, the optimal range of concentrations and toxicity of high doses.

This is particularly well illustrated in numerous experiments: when added to animal food small amounts of oregano and pine EO (or fresh herbs of these plants) an increase in fertility, reduction in mortality among young individuals, accelerated weight gain, stimulation of the immune system and improvement of the epidemiological situation in herds were observed [5].

Adding sage, clove or cinnamon EO in the amount of 0.25% and Origanum oil in 0.1% within 2 weeks in female mice food was accompanied by embryotoxic effect - reduction in number of dividing cells and increase of dead cells in the embryos. Concentration of the oil was so high that the animals refused to eat food.

Most of EO authorized for use forms a group of little and virtually non-toxic substances.

According to our data, LD50 for EO of Monarda and eucalyptus was 360-600mg / kg by inhalation and 600-1200 mg / kg intraperitoneal injection for guinea pigs. In the studies of chronic toxicity dystrophic changes of internal organs, pathological changes in the kidney, spleen, peripheral blood and immunosuppression were observed in the animals.

But the dose of EO could be a matter of choice under extreme conditions: in the animals irradiated with a lethal dose of γ -rays observed protective effect of inhaled course with essential oil vapors at concentrations of 20-100 mg / m³ of air [3].

However, we recommend not creating concentration of EO in the air more than 5 mg / m³ during the aromatherapy. From our point of view 1-3 mg / m³ EO concentration in the air at the session duration for 20-25 minutes are optimal.

But the dose of EM can be a matter of choice under extreme conditions : in the animals irradiated with a lethal dose of γ - rays observed protective effect of inhaled course with essential oil vapors at concentrations of 20-100 mg / m³ of air [3].

Conclusions

Natural EO are widely used as an independent and additional medicaments for the treatment and prevention of various diseases and syndromes.

Aromatherapy procedures requires special training of employees as knowledge of chemistry, toxicology and safety in the use of EO are needed.

Before the appointment of aromatherapy it`s necessarily to conduct tests on individual tolerance. Complaints of cough, shortness of breath, skin redness, itching, rash, etc. are the contraindications for this patient taking EO therapy.

High concentrations of EO are toxic for humans and animals.

EO should only be stored in glass containers away from light and air. If not properly stored essential oils lose their therapeutic properties and get allergens` properties.

Mixtures of 2-3 oils should not be stored and used for over a year. Using of multicomponent mixtures is not recommended due to unpredictable changes in their chemical composition and pharmacological properties.

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Essential oils are used as an independent as auxiliary medicines for the treatment and prevention of various diseases and syndromes.

The review of the literature contains data about essential oils contents, therapeutic concentration and rules of use in medical practice. The article also covers different points of views in usefulness, harmlessness and dosages of essential oils. The particular attention is paid to safety making a prescription of the aromatherapy: storage precautions, dosages, toxicity, allergenic capacity, ability to use essential oils with medicines. The information is given for practicing physicians.

Keywords: essential oils, composition, contraindications, dosages, toxicity.