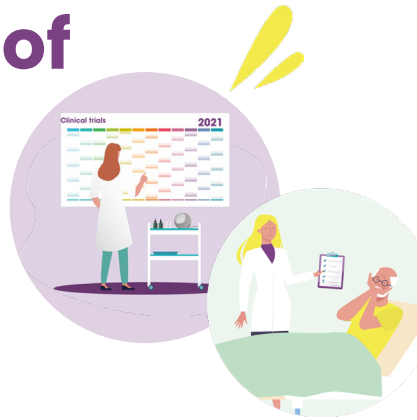
Fondation Gattefossé
pour l'aromathérapie clinique

Need to improve the quality of clinical studies in Aromatherapy



By the scientific board of the Gattefossé Foundation: Robert Anton, Sabrina Boutefnouchet, Philippe Colls, Françoise Couic-Marinier, Jacques Kopferschmitt et Jean-Michel Morel

"*Breathing in the smell of lavender essential oil does me such good!*" reports a patient. Does this provide sufficient evidence to claim that aromatherapy is an effective complementary therapy? Clearly not.
In order for aromatherapy to be recognised as a complementary approach, we need to develop clinical research that provides evidence of efficacy and safety.

Clinical aromatherapy consists of using essential oils, notably for their anxiolytic, analgesic and antiseptic and other such properties, to relieve a patient's symptom. This approach is primarily used to complement drug treatment and is prescribed by a healthcare professional with training in aromatherapy.

While the outcome may be appreciated by the patient and the prescriber, a single observation is not enough to gain the trust of peers, the authorities and the general population. Aromatherapy would benefit a great deal from complying with the requirements of evidence-based medicine (EBM).

Over the years, as members of the **Gattefossé Foundation** [1] Scientific Board, we have observed an increase in the number of healthcare professionals practising clinical aromatherapy, as reflected in the many grant applications received to implement such protocols in French hospitals. We are delighted to see clinical aromatherapy finding its place in integrative medicine. Yet despite the many benefits patients receive from these protocols, some decision-makers are cautious about offering this complementary therapy due to a lack of knowledge and high-quality clinical studies.

Why? This is largely because of problems with the methodological quality of the published clinical studies. The systematic reviews published by the **Cochrane** network [2] conclude that most clinical studies of aromatherapy produce poor-quality evidence or even no evidence due to problems such as flaws in their design or presentation and low statistical power. In a recent scoping review assessing the extent of evidence for aromatherapy in nursing published since 2005, only 124 references were included [3].

In order to achieve greater recognition of clinical aromatherapy as a complementary approach, it is important for all contributors to be aware of these limitations when publishing their clinical research.

This white paper provides a reminder of the essential points to consider when reading academic papers, to recognise the quality of the study being reported, and to identify all the key points to take into account in order to build more effectively on these results. It is aimed at anyone wanting to conduct clinical research in aromatherapy.

By working together, we can ensure that clinical aromatherapy receives greater recognition.

#1 A detailed description of the 'aromatic' protocol

Providing a description of the conditions of the intervention is one of the key prerequisites for a clinical study. This description must reflect the practice used in detail, and enable other research teams to reproduce the protocol, confirm the results in order to carry out comparative studies and ultimately facilitate meta-analyses.

Unfortunately, we have found that most aromatherapy papers do not contain the information required for a full description of the intervention.

Essential oils are natural products derived from aromatic plants and, with the exception of citrus essential oils (Citrus sp.), are mainly obtained by steam distillation.

They contain hundreds of different molecules, derived from a few large basic molecular groups with variations in function. As their composition varies from one season to another, from one region to another and from one plant to another, it is important for research articles to provide a detailed description of each of the essential oils used

Due to the wide variability of essential oils, it is essential to provide a description of them that includes information about numerous characteristics [4-6]

The complete characteristics of essential oils consist of:

1 / Their scientific name (Latin name, author, botanical family of the original source material)

2 / Their geographical origin

3 / The extraction method used

4/Their specific biochemical characteristics or chemotype

5/ The name of the producer and supplier, and the batch number

6/ Their exact composition (gas chromatography profile) to be added as an appendix to the study

NB: The same requirements apply when using a blend pre-prepared by a manufacturer (list details of each essential oil used)

A detailed aromatherapy protocol is one of the prerequisites for making the results reproducible

The description of how the essential oils are used and administered must include details of:

1/ The aromatic preparation incorporating the essential oils and the carrier oil or excipient used, with the concentration expressed in milligrams, volume or as a percentage

2/ The route of administration and protocol for use (dose, application surface area, duration, frequency)

3/ Safety information (quantity of essential oil/dose unit, list of contraindications) [7]

A lack of information and description of the intervention represents a major barrier to validating the results of a study. Authors need to be aware of these universal limitations, as they have a major impact on the quality of a study.

Two international initiatives currently provide valuable resources for authors. The first of these is the **CONSORT** [8] (Consolidated Standards of Reporting Trials) Group, a collaboration synthesising the work of specialist clinical trial methodologists. The group produces guidelines for reporting clinical trials, and has published recommendations for reporting randomised controlled trials of herbal interventions [9]. These recommend providing information on the same characteristics when describing the intervention.

4A – Herbal medicinal product name

4B - Characteristics of the herbal product

4C - Dosage regimen and quantitative description

4D - Qualitative testing

CONSORT Group recommendations

The second international group, **ARQAT** [10] (Aromatic Research Quality Appraisal Taskforce) develops, evaluates and writes guidelines for defining the quality standards applying to clinical aromatherapy research reports. This group recently developed the TREATS (Transparent Reporting for Essential Oils & Aroma Therapeutic Studies) tool, which can be used to evaluate the quality of a published study against a list of specific parameters. It lists the same characteristics. The quality of a publication is thus primarily based on a proper description of the aromatic protocol [11].

Article reviewed:			
Category	**Meets (yes, N/A)**	**Does Not Meet**	**Comments/ Questions**
Essential oils (EO)/ Carriers			
Name including botanic (Latin)			
Supplier			
Extraction method			
Country of origin			
Date purchased			
Batch number			
Complete listing of constituents (link or attachment)			
Dilution			
Carrier(s) details on purchase			
Control			
Odor bias questions			
Odor recognition			
Odor preference			
Too strong or weak			
Irritating or non-irritating			
Previous use of EOs/expectations			
Allergic reactions to EO/aromas			
Test for anosmia			
Aromatherapy			
Description of aromatherapy			
Professional aromatherapist consulted (Qualifications)			

Before conducting a clinical study, a literature review of the latest research should be conducted. The TREATS checklist helps to assess the quality of evidence in the existing literature.
To validate this tool, ARQAT evaluated a large number of articles and systematic reviews. From the three reviews selected from the Cochrane database [12-14], the quality of ten studies was critiqued using TREATS and found to be suboptimal from the standpoint of reporting aromatherapy/ essential oil interventional research.

#2 The choice of evaluation method

Here we refer solely to clinical studies in humans, since in vitro and animal studies are prospective or preclinical studies that are simply used to develop hypotheses of action and can in no way be used to produce evidence of efficacy in humans. The main purpose of a clinical trial is to evaluate the therapeutic value of a treatment or to measure the benefit to the patient and validate safety.

Many different methodologies are now available. The simplest, but least powerful, of these is the observational method, which demonstrates the efficacy of a therapy in a cohort of patients with a common pathology. These often consist of case studies that include only one group of patients. Many papers report studies of this type. This approach remains very useful if the description of the intervention follows the rigorous guidelines outlined above.

An alternative methodology is the 'interventional' study, usually referred to as a clinical trial, the objective of which is to demonstrate the safety and efficacy of a therapy by comparing the effects obtained in a group of patients receiving the therapy with another group of patients receiving a different therapy (control group). In general, for it to have sufficient statistical power, the study must be a randomised controlled trial (RCT), i.e. one in which the patients are randomly assigned to one group or the other. This means that the higher the number of patients, the more significant the statistical evaluation of the comparisons of means and standard deviations.

The 'gold standard' clinical trial is double-blind, enabling objective group selection, since neither patients nor care providers know who is in the intervention group and who is in the control group.

When working with odorous products such as essential oils, a double-blind model is very difficult to implement unless the control group uses another odorous substance.

In practice, evaluations of Non-Pharmaceutical Interventions (**NPIs**), such as aromatherapy, have to adapt these methodological designs that have been developed for evaluation of drugs. The NPIS [15] (Non-Pharmacological Intervention Society) was established by Prof. Grégory Ninot in 2021 to bring together and develop shared tools for evaluating NPI, with a view to increasing their acceptance and integration in healthcare systems.

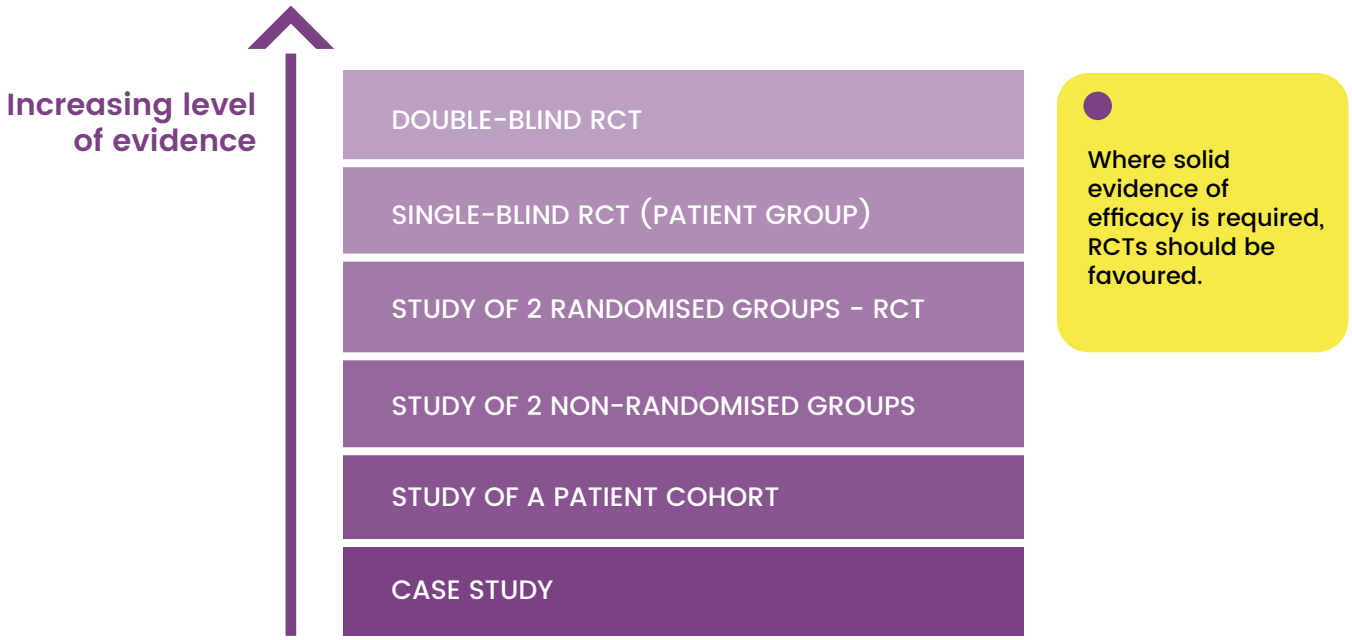
There is no special 'aromatherapy' methodology. The benefit to the patient must be evaluated by conducting the most rigorous study possible with the resources available. Aromatherapy research must be conducted along the same principles as conventional clinical research.

Today, practicality is essential, and studies should be conducted using a reproducible evidence-based method that addresses a specific problem. For example, if the question asked is 'Does aromatherapy help the patient feel better?', it may not be necessary to compare the intervention to a placebo group. Conversely, if the question asked is 'Does aromatherapy have a specific effect, which improves the patient's health (beyond a placebo effect)?' then such a comparison is necessary. Use of a placebo should be considered to increase the robustness of the evidence produced.

It is important to understand that the demonstration of efficacy is based on comparative statistical analysis. Where it is not possible to compare two groups (numbers too small, high cost, insufficient resources), it can be useful to conduct a case study on a cohort of patients that is as homogeneous as possible (= same therapy, same pathology and same symptoms) to avoid subjectivity and obtain a sufficiently large group size to observe a mean / median and have data on intra-group variability at the very least. Care must be taken when drawing conclusions in a paper regarding the validity of a positive result for a single group of patients. This type of study is, however, often unfairly discredited, and is currently undergoing a certain re-appreciation.

In a single - or double- blind study, it can be useful to administer a synthetic fragrance-type placebo to draw conclusions regarding the specificity of the effect of the essential oil and its components. However, care must be taken not to compare fragrances that can trigger a 'Like/Dislike' effect between groups.

Single or double-blind aromatherapy studies remain difficult to implement and are not mandatory: a non-blinded randomised study may be sufficient to prove the benefits of aromatherapy by comparing two groups.



Where solid evidence of efficacy is required, RCTs should be favoured.

#3 Endpoints

The choice of endpoints is crucial. Careful consideration must be given to this decision when evaluating symptoms such as pain, anxiety, nausea and well-being, as numerous published studies present ambiguous results in relation to these aspects. There are two types of evaluation: quantitative and qualitative.

Quantitative studies produce numerical results derived from a physical or biological measure or a validated scale / patient reported outcome (PROM). Where possible, we recommend using measurable endpoints such as the level of a biomarker (cortisol, dopamine, cytokines IL-2/IL-10), microbiological analyses, or any quantifiable measure (such as days of hospitalisation, number of pain killers or hours of sleep). Skin healing can also be easily evaluated and measured. Ideally this data would be triangulated with data from a validated PROM to help assess safety and subjective benefit.

In aromatherapy, however, many of the efficacy endpoints involve the measurement of anxiety, pain or well-being, which are subjective to the patient. For many years, these endpoints were considered to produce low-quality evidence, since they are non-reproducible from one individual to another and even sometimes in intra-individual terms. Now, however, numerous standardised questionnaires are available, using standardised criteria that facilitate their inclusion in a scientific approach.

Pain can be measured using self-assessed numerical scales (NRS) or visual analogue scales (VAS) and standardised and validated questionnaires (BPI) [16-17]. Two pain rating scales have been developed for elderly people with verbal communication difficulties: **Doloplus, Algoplus** [18].

Anxiety can also be measured using rating scales. The most used self-administered questionnaires are the Spielberger STAI (Spielberger State-Trait Anxiety Inventory) [19-20], the Hospital Anxiety and Depression scale (HAD) [21], the Hamilton scale [22-24] and the GAD 7 (Generalised Anxiety disorder assessment) [25].

Sleep disorders can be measured using the Insomnia Severity Index (ISI) [26] or the Pittsburgh Sleep Quality Index (PSQI) [27].

Some research groups have shown that several scores can sometimes be combined to confirm a subjective parameter relating to levels of anxiety and thus reduce measurement bias [28].

In evaluations of a complementary therapy, Prop the patient's lived experience plays an essential role, and this field is increasingly producing **qualitative studies**, which consist of gathering opinions, comments and verbal data from patients (semi-structured interview). These studies explore patient-reported outcomes (MYMOP [29], MyCaW (30]) using non-numerical, non-measurable endpoints. As such, the results obtained do not allow for statistics-based conclusions. They are based on patient subjectivity and provide evidence of the patient's lived experience.

The qualitative approach is increasingly popular in France, and France's National Institute of Health and Medical Research (Inserm) is collaborating with a qualitative medical research group on a method called the IPSE (Inductive Process to analyse the Structure of lived-experience [31]).

The French National Authority for Health (HAS) also carries out real-world research to evaluate the utility, effectiveness and impact of drug treatments on patient quality of life [32]. This also makes it possible to uncover 'disutility', which is when patients experience excessive adverse effects, including in physical, psychological and social terms.

The qualitative approach is highly appropriate for aromatherapy and may be used alongside a quantitative methodology. It can even be useful for establishing the prerequisites for a quantitative study and to determine the appropriate efficacy endpoints.

#4 Statistical power

Many studies are based on too small a number of patients. Collaborations between institutions should be considered as a way to increase the number of patients involved and thus improve the statistical significance of the results. These would require the development of standardised, shared protocols via professional networks, which would facilitate multi-centre studies. Numerous clinical conditions lend themselves to this approach, including anxiety, sleep disorders and pain, but several more specific clinical situations (such as infectious diseases) would also benefit from studies with greater numbers of enrolled patients.

Although the therapeutic value of aromatherapy has been understood and recognised for thousands of years, we must all work together to validate its safety and measure its benefits in a rigorous, scientific way. This is the only way to ensure that aromatherapy secures its rightful place.

To achieve this, physicians, clinicians, pharmacists, nurses and therapists need to continue to evaluate the benefit experienced by their patients and publish their clinical findings in line with best practice in order to build a high-quality evidence base.

The scientific quality of a publication is based on the reproducibility of the observed facts, which requires a clear description of the study conditions. It is therefore essential to provide a detailed description of the fixed study parameters, which consist of the essential oils used and the method of administration. Patient subjectivity provides more than enough variability to deal with alongside these fixed parameters. A rigorous description of the 'aromatic' protocol is a must, otherwise the study is not reproducible and its conclusions cannot be further developed.

The choice of methodology needs to be pragmatic, but where possible we advise using a model able to produce the highest possible level of evidence.

The choice of endpoints is also crucial. Qualitative studies appear to be well suited to the evaluation of clinical aromatherapy as a complementary therapy, in response to the collateral effects of disease (such as anxiety, insomnia, stress and pain).

As members of the Gattefossé Foundation Scientific Board, we are committed to this endeavour, and fully support recent initiatives to promote guidelines designed to help practitioners develop aromatherapy with their patients in a safe setting [33] and to improve the quality of clinical research and publications.

If we do not develop this collective awareness, the quality of the published evidence will not allow us to build what is required to legitimise aromatherapy as a complementary therapy within integrative medicine: an evidence-based aromatherapy.

By working together, we can support patient well-being by ensuring that the value of clinical aromatherapy is properly recognised.

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'At the heart of integrative medicine, the Foundation is committed, in France and abroad, to developing clinical aromatherapy to improve patient care.

The Foundation works by encouraging clinical research, encouraging its practice in hospitals in France and promoting aromatherapy practitioners and their clinical experience.'

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