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Classification of systems and methods used in biological basic research on homeopathy

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The HomBRex database indexes basic research on homeopathy (www.carstens-stiftung.de/hombrex). It includes research on effects of homeopathic preparations in bioassays and physico-chemical effects of the homeopathic preparation process (potentization). At the end of 2006 it contained more than 1100 experiments in more than 900 original articles, including 1014 biological studies. The types of organisms used as laboratory "model" organisms in fundamental homeopathic research include animal, human, plant, fungi and microbial organisms. Most animal studies (607) were with rats (209) or mice (171). Most plant studies (171) were with wheat (52). The database catalogues whether the experiment was performed on intact organisms or in organs or cells, isolated and analyzed for changes in structure, function and subcellular composition. The database might be especially useful to facilitate a search for experimental models that have been used in the study of both proving and therapeutic experiments—ultimately in the research on the homeopathic similia principle. *Homeopathy* (2007) **96,** 247–251.

Keywords: homeopathy; basic research; database

Introduction

The 200-year-old therapeutic system of homeopathy uses small doses (potencies) of a variety of substances to stimulate auto-regulation and self-healing processes of patients based on the 'similia' principle. A substance is chosen if it provokes, in a healthy subject, symptoms requiring treatment in a diseased subject. Fundamental research has studied, in laboratory 'model' organisms, basic mechanisms underlying homeopathy. Such models mimic both the clinical experience of human subjects and the clinical application of homeopathic substances.

A laboratory model should provide a means to explore issues of homeopathy within the present mainstream biological and biomedical paradigm. Thus, the ideal laboratory model should provide the opportunity to study the following:

a. a proving: the response of a healthy organism when exposed to a substance; and
b. the effect of a substance on the diseased state of a 'patient' organism.

As a basis for studying the use of healthy and diseased organisms as laboratory models in fundamental studies, we first conducted an overview of all biological organisms previously reported in the literature.

The database on fundamental research in homeopathy[1] was based on this review. This paper provides, in an explorative and quantitative way, a new overview on the state of the database and, in particular, on the characteristics of laboratory models. The paper provides: (a) background information helpful in information retrieval from the database and (b) assistance in planning new research.

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Table 1 Analysis of experiment

Question	*Answer*
Object under study	
What is the type of organism under study?	Animal, human, plant, fungus, microbial
What is the kind of organism under study?	Rat, mouse, etc.
Is the object of study the whole organism or a specific part?	Organism, organ, cell, subcellular structure
Is the substance administered in vitro?	Yes/No
Field of science	
To which field of science belongs the experiment?	Anatomy, immunology, physiology, etc.
Condition of object	
Is the object in a special (not healthy) condition?	Infection, intoxication, irradiation, cancer, diabetes, etc.
Is the non-healthy condition spontaneous or induced by pretreatment?	Spontaneous/induced
Parameters under study	
Which main parameter is studied?	Growth, survival, morphology, etc.
Substance under study	
Which substance is studied?	Name of substance
Which dilution is studied?	Dilution of starting material (eg 10^{3}, 10^{6})
Is the substance diluted only or potentized?	Dilution/potency
Which type of potency is studied?	D, C, LM, K
Is the substance tested as high potency (>D23 or C12)?	Yes/No
Design of study	
Is the study blind?	Yes/No
What type(s) of control is utilized?	Placebo, potentized placebo, etc.
Specialties	
Is any of the following principles studied: similia principle, isopathy, hormesis?	Yes/No

Methods

The authors have established an archive, the HomBRex (Homeopathy Basic Research experiments) database.[1] The publications in the database report exclusively original experimental work in basic homeopathy research. The database and archive were compiled under supervision of one of the authors (HA) by experts both in software and library and information systems. The database address is http://www.carstens-stiftung.de/hombrex.

This archive is updated continuously by systematic searching of bibliographic databases, reference lists of new review articles and hand searching of homeopathic journals.[1] Only the initial experiment publications is indexed, so not every publication on basic homeopathy has been included. The literature is screened for duplications as well as review articles to assist the user in finding the original publications. The inclusion of initial publications is not time-limited: research from the 19 century is included. Languages are English, German, French, Dutch, Italian and Spanish. Although the experiments deal with homeopathy, only part of the information has previously appeared in homeopathy journals. Some of the experiments appeared in the pharmacological and toxicologial literature. Since this literature has not yet been systematically searched for low dose effects, some of these experiments may be still unnoticed. Proving studies and clinical trials were not included in this database.

Each original publication is analyzed for its main experimental questions. In several publications, more than one experimental question is addressed. As of December 2006, the database contained more than 1100 experiments in more than 900 original articles. Data extraction and cross checking was supervised by one of the authors (HA) and carried out by scientific coworkers. Each experiment was analyzed for:

a. the subject under study,
b. the condition of the subject,
c. the substance(s) under study,
d. the parameters for recording any effect of a substance,
e. the field of regular science to which the study belongs
f. the design of the study. The analysis is summarized in Table 1. The substances are categorized according to Schroyens.[2]

Results

An extrordinary diversity of model systems has been examined in fundamental homeopathy research. The research includes investigations of: biological systems ranging from complex, multicellular organisms (i.e., mammals and plants) to single cell organisms and intact organisms to isolated cells and subcellular structures. An overview of the types of organisms and isolated parts of organisms that were used in the experiments is presented in Table 2. The majority of experiments were carried out on animals; the second largest group is with plants. Complex, multicellular organisms (animal, human and plant systems) were

tested as whole or parts of systems either after isolation or in vitro culturing (eg, as isolated organs or cultured cells). The majority of experiments with animals and plants were with intact organisms.

Human experiments in the category 'intact organisms' are neither pathogenetic nor clinical trials. Rather, this category includes human experiments that were considered by the authors as basic research; eg, the action of low dose acetylsalicylic acid (aspirin) in healthy volunteers. In the animal and human categories, experiments using 'organs in vitro' include both organs and blood. The human experiments in this category are all with blood. In animal experiments, the percentage of experiments using 'cells in vitro' was considerably higher than in plant experiments. In studies with human systems, the percent of studies using 'cells in vitro' was the highest.

The 35 studies with simpler eukaryotic organisms in the 'fungi' category can be divided into categories: four with fungi not in artificial culture but under natural conditions; 31 in vitro culture. The 37 experiments with microorganisms included: six with microorganisms, not in artificial culture, and 31 in vitro experiments.

A total of 34 animal species and 51 plant species were utilized in fundamental homeopathy studies. The top 10 animal and plant organisms are presented in Table 3. In experiments with animals or part of animals, the favorite animals were rats (213 experiments or 35%) and mice (175 experiments or 29%). In experiments with plants, the favorite organism was wheat (72 experiments or 37%).

Experiments have been carried out with intact organisms or with isolated parts such as organs, cells or subcellular structures. When focusing on intact organisms only, the question has been asked what parts of the intact organisms have been studied to characterize the effect of substances administered to intact organisms. Effects were measured either at the level of the entire organism (using parameters like behavior, body temperature and mortality), at the level of organs (isolating one or more organs to characterize changes in histology, enzyme activity, etc.), at the level of cells (isolating cells to estimate growth, cell motility, etc.) or at the level of subcellular structures (isolated molecular constituents such as enzymes). Table 4 presents information about the different levels of observation to characterize the effect of substances in the entire animal, human and plant organisms. Most studies dealing with such organisms focused on the characterization of effects at the organ and cellular level. In several experiments, measurements at more than one level were made.

Research in fundamental homeopathy has been done in many biological disciplines. Its link to the major disciplines are shown in Table 5. In addition, a substantial number of homeopathic studies were found in biomedical disciplines such as neurophysiology, psychophysiology, immunology, oncology, pharmacology, toxicology and traumatology.

Table 4 Levels of observation to characterize the effect of substances in entire organisms

Type of organism	*Level of observation*			
	Intact	*Organ*	*Cell*	*Subcellular structure*
Animals	184	300	0	0
Human	12	48	15	0
Plants	96	128	0	2

Table 2 Number of experiments with animals, humans, plants, fungi and microorganisms; substance being given to the biological systems ranging from intact to subcellular structure

	Total	*Intact organisms*	*Organs in vitro*	*Cells in vitro*	*Subcellular structures*
Animals	607	451	58	75	23
Human	164	65	10	84	5
Plant	171	129	28	3	11
Fungi	35	35	N.a.	N.a	0
Microorganisms	37	37	N.a.	N.a.	0

Table 3 Top 10 animal and plant species used in fundamental homeopathy experiments

Top 10	*Animal species*	*Animal—number of experiments*	*Plant species*	*Plant—number of experiments*
1	Rat	213 (34.8%)	Wheat	72 (37.5%)
2	Mouse	175 (28.6%)	Gladiolus	11 (5.7%)
3	Guinea pig	40 (6.5%)	Pea	9 (4.7%)
4	Frog	35 (5.7%)	Potato	8 (4.2%)
5	Rabbit	32 (5.2%)	Cucumber	8 (4.2%)
6	Pig	31 (5.1%)	Lentil	5 (2.6%)
7	Chicken	27 (4.4%)	Tobacco	5 (2.6%)
8	Cow	14 (2.3%)	Cress	5 (2.6%)
9	Toad	5 (0.8%)	Onion	4 (2.1%)
10	Eel	5 (0.8%)	Tomato	4 (2.1%)
Others		34 (5.6%)		51 (26.6%)

Table 5 Number of experiments in fundamental homeopathy by fields of science

Scientific field	*Number of experiments*
Biochemistry	100
Cell biology	165
Developmental biology	41
Immunology	155
Microbiology	53
Neurophysiology	47
Oncology	28
Pharmacology	154
Physiology	368
Psychophysiology	29
Toxicology	188
Traumatology	25
Virology	23

Discussion

Overall, the database reveals that research on homeopathy is still in a state of exploration. Approximately 1100 experiments over 100 years are distributed over most biologic and basic science fields. They deal with many kinds of organism, living material and as many as 700 substances in a wide range of potencies or dilutions.

The great variability originates from methods with which the primary investigators were familiar. If a line of research is part of a conventional research program, the experiments by the research team commonly aimed to establish which experimental conditions would determine the outcome of a particular experiment. The experimental conditions that must be controlled to attain a constant outcome are many. Continuing research within a particular team is the primary way to establish these conditions. Thus, the protocols for basic homeopathic research are still developing. It is too early to call for systematic replication or confirmation of certain experimental designs. There have been few attempts to repeat certain experiments, particularly those published in high profile journals.[3,4] Nevertheless, this database reveals some confirmative research which one might call 'unconscious reproductions'. One example is in vitro experiments with isolated rat ileums that have been, at least four times, independently conducted over a period of 60 years.[5–8] In the future, the database should prevent such 'unconscious repetitions'.

Historically, quality measurements have been attempted three times, all utilizing conventional, clinical trial based scoring instruments.[9–12] From the authors' perspective, this approach did not meet the special challenges of basic homeopathic research. Two major distinctions between human homeopathy trials and basic studies with cells and enzymes are: the placebo effect and the doctor–patient interaction effect. Experimental studies in cell culture and enzymes have many pitfalls, but do not include psychological factors.

However, the marked variability of the results within and between various in vitro studies of homeopathy requires other explanations. Quality measurements must be included amongst the experimental conditions. This, however, requires detailed knowledge of organisms and examination of research methods/protocols by specialists in the corresponding fields of research. Wider acceptance of quality measurements with clinical trial based scoring instruments plus peer review processing of research has increased respect for clinical trials in the last decades. Unfortunately, publications prior to 1990 were often not subject to peer review. However, discussion on experimental methods in basic homeopathic research is urgently needed. The present status of quality-scoring instrument may misrepresent the actual state of knowledge in such research.

It can be argued that basic research models should contribute to the understanding of the Similia Principle. An ideal model for such study would be: (a) characterized in pathogenetic trials, (b) characterized in terms of its diseased, disordered or toxic states and (c) treated with a substance selected according to the Similia Principle using data from both proving and diseased state studies.

The most important conclusion from the initial overview of existing basic research is that rat and mice (in animal systems) and wheat (in plants) should be the major foci. In another paper, the authors analyzed the database from the perspective of proving and therapeutic studies.[13]

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