

RESEARCH REVIEW

Infection models in basic research on homeopathy

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Introduction: The objective of this study was to search for effective agents for the treatment of infections in animals or infected cell lines.

Methods: The Homeopathic Basic Research experiments (HomBRex) database (<http://www.carstens-stiftung.de/hombrex>) on model biological systems in homeopathic research was searched. Eligible experiments were reviewed and analysed.

Results: The database contains 48 eligible experiments published from 1832 to 2009. Causative pathogens were bacteria, fungi, viruses, proto- and metazoa. In the experiments, various parameters were observed and a large set of medicines was investigated. In eight of the 48 experiments, at least one of the investigated medicines was selected according to the similia principle. Nosodes and homeopathic complexes were investigated in 8 and 14 experiments respectively. Mice were the most often used host organisms (13 experiments). In 31 experiments at least one homeopathic medicine was found effective for treatment.

Conclusion: The results of basic research experiments may invigorate new clinical trials that investigate complementary treatments for infectious diseases. However, all experiments reviewed here await replication and no clear-cut conclusion can be drawn regarding the transferability of *in vitro* results to *in vivo* outcomes. *Homeopathy* (2010) 99, 263–270.

Keywords: Basic research; Database; Homeopathy; Similia principle; Infections

Introduction

In homeopathy, practitioners treat diseases using very low dose preparations (potencies) according to the principle “*let like be cured by like*” (*similia similibus curentur*): homeopaths select a drug that would, if given to a healthy person, cause symptoms similar to the presenting symptoms of the patient. This “*similia principle*” is the cornerstone of homeopathy. Fundamental research in physico-chemical experiments or laboratory model organisms has studied the basic mechanisms underlying homeopathy and the similia principle. The HomBRex database (Homeopathy Basic Research experiments) comprises a large set

of such experiments^{1–3} (<http://www.carstens-stiftung.de/hombrex>).

In April 2009, a total of 1359 experiments, published between 1832 and 2009 in different fields of homeopathy basic research, were registered in the database. Of these experiments, 606 dealt with organisms that were ‘suffering’ from some kind of condition. Most of these conditions represented some negative pathophysiological state (therefore ‘suffering’) for the investigated organism and homeopathic drugs were examined whether or not they were able to alleviate this diseased state. Most of these conditions were induced ($n = 505$); some were spontaneous ($n = 98$) and represented natural situations in the life-cycle of the particular organisms. In three experiments, the origin of the conditions were unknown.

For this publication, we reviewed the current state of homeopathy basic research aimed at finding effective agents for the treatment of organisms infected with bacteria, fungi, viruses, proto- and metazoa (*condition = infection*). Reasons for this selection were: (1) a search in the

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HombRex database revealed that *infection* is the second most common term ($n = 80$) in the category *condition* after *intoxication* ($n = 208$), the next most frequent is *cancer* ($n = 51$); (2) in contrast to our recent article on rats in basic research,⁴ where most experiments dealt, in fact, with isopathy, we expected a larger number of experiments based strictly on homeopathy (using similar, not identical, curative agents) and therefore further substantiated the similia principle; (3) the treatment of infections is very important, clinically.

Many conventional therapies for infections caused by viruses, bacteria, fungi or proto- and metazoa may, despite being effective, cause adverse events^{5–9} and there is great interest in finding alternative treatments of low toxicity for such diseases. The results of basic research experiments may inspire new clinical trials that investigate such alternative treatments.

Methods

The HombRex database (<http://www.carstens-stiftung.de/hombrex>) and analysis of the data it contains were described elsewhere.^{1–4} Human pathogenetic trials (provings) and clinical trials are not included in the database. The analysis of the database for this study was conducted in April 2009. All experiments applying plants, animals and humans infected with viruses, bacteria, fungi, proto- and metazoa published between 1832 and April 2009 were included. Search parameters were organism (*animal, fungus, human, microbial, plant*) and condition (*infection*). This excludes inoculations with cancer cells that might be misunderstood as infections. Inflammations induced by inflammatory chemical agents and experiments based on antiviral, antifungal or antibacterial action of homeopathic medicines tested directly on free-living pathogens (without a host organism) were also excluded.

Results

The database search revealed 80 experiments with organisms infected with viruses, bacteria, fungi, proto- and metazoa. More than one-third of the experiments ($n = 32$) deal with infected plants. These were excluded, because most of these experiments have already been recently reviewed.¹⁰ In the remaining 48 experiments, intact animals ($n = 33$), animal cell lines ($n = 7$) and human cell lines ($n = 8$) were investigated. Of the 33 experiments with intact infected animals, six were excluded in the subsequent investigation because they did not focus on the treatment of the respective infections, leaving a total of 42 experiments for analysis (27 infected animals, 7 animal cell lines, 8 human cell lines). No experiment used rats, in contrast to the conditions *intoxication* and *cancer*, wherein almost half of the experiments were performed with rats (according to a search request in HombRex and see Ref. 4).

In eight experiments, at least one of the investigated medicines was selected according to the similia principle (from *Materia medica* and/or repertory) as outlined by the authors

(field remarks, Tables 2–4). In 12 experiments, some of the investigated medicines were only selected because of previously published or traditional positive results (e.g. in the field of phytotherapy). In five experiments, the authors did not comment on remedy selection. Eleven experiments were on homotoxicology. Nosodes (with regard to isopathy) and homeopathic complexes were investigated in 8 and 14 experiments, respectively.

Experiments with intact infected animals

In 34 experiments with animals ($n = 27$) or animal cell lines ($n = 7$) published in 26 publications (Table 1), mice were the most often utilised model organism ($n = 13$) followed by chickens ($n = 9$) and dogs ($n = 5$). In mice and chickens, primarily intact organisms were investigated. In the 12 experiments with intact mice as model organism, a large number of medicines were tested in the treatment of infections by viruses, proto-/metazoa and bacteria (Table 2). All but one¹¹ infections were induced. In two experiments,^{12,13} the authors selected some of the investigated medicines according to the similia principle (with positive results). Unfortunately, Jonas¹² does not state what medicines, besides the nosode, were used (“*several commercial homeopathic preparations*”) and does not show any numerical data regarding the efficacy of these commercial preparations (“*mild degree of protection*”). Overall, in 10 experiments at least one of the ($n > 20$) investigated medicines was reported effective in the treatment of the respective infection (Tables 1 and 2). Best results were reported for the treatment of the nematode *Trichinella spiralis* with *Artemesia cina* (*Cina*) (about 85% reduction of larvae in muscle tissue)¹⁴ and for the treatment of Leishmaniasis (about 90% reduction of the diameter of the lesions).¹⁵

In chickens, only bacterial and viral infections were investigated in nine experiments (Table 3). Eight infections were induced. Only Sandoval *et al.* investigated spontaneous salmonellosis in 800 chickens¹⁶ (remedy selection was based on the similia principle). Homeopathic treatment with *Baptisia* (*Bapt.*) (30c) was reported to be as effective as the standard treatment with Ciprofloxacin. Velkers *et al.* have investigated various combinations of homeopathic

Table 1 Number of experiments with different infected animal models or human cell lines

Organism	Intact organisms		Cell lines		Reference*
	n	Pos./Neg.	n	Pos./Neg.	
Mouse	12	10/2	1	0/1	11–15, 19, 20, 33, 44–46, 58
Chicken	9	8/1	0	–	16–18, 20, 21
Dog	1	1/0	4	1/3	22, 28–31
Monkey	0	–	2	1/1	31, 33
Guinea pig	2	1/1	0	–	26, 27
Sheep	1	0/1	0	–	24
Cow	1	1/0	0	–	25
Rabbit	1	1/0	0	–	23
Human	0	–	8	7/1	28–32

n = number of experiments.

* Some references contained more than one experiment.

Table 2 Summary of infection experiments in mice

Pathogen	n	Therapeutic substances	Potency range	Observed parameters	Result	Remarks*	Reference**
<i>Leishmania braziliensis</i>	1	<i>L. braziliensis</i> (nosode)	30 and 200 (c and d)	Size of lesions	Pos.		15
<i>Trichinella spiralis</i>	1	<i>Cina</i> , <i>Santin.</i> , <i>Podo.</i>	∅ and 30c	Number of larvae in tissue	Pos.	Korsakoff-potencies	14
<i>Plasmodium berghei</i>	1	<i>Eup-per.</i> , <i>Ars.</i>	30c	Number of infected erythrocytes	Pos.	Similia principle. Another but undefined potency was used	13
<i>Trypanosoma cruzi</i>	1	Blood-nosode, <i>T. cruzi</i> (nosode)	10d and 30d	Histology	Pos.		45
<i>Streptococcus</i> sp.	1	Ergot alkaloids	--	Mortality	Pos.	No potencies, only very high dilutions	58
<i>Francisella tularensis</i>	2	<i>F. tularensis</i> (nosode), various other, not-specified substances	3–14d; 30–1000c	Mortality	Pos.	Similia principle. ¹² High-quality study design and evaluation	12,44
Coxsackie virus B4	1	Complex drug (see Table 7)	--	Titer of viruses in pancreas	Pos.		33
Simliki Forest Virus (SFV)	2	<i>Aconitum napellus</i> (<i>Acon.</i>), <i>Ranunculus bulbosus</i> (<i>Ran-b.</i>), <i>Bothrops lanceolatus</i> (<i>Both.</i>), <i>Rhus toxicodendron</i> (<i>Rhus-t.</i>), <i>Eupatorium perforatum</i> (<i>Eup-per.</i>), <i>Pulsatilla</i> (<i>Puls.</i>), <i>Psorinum</i> (<i>Psor.</i>), <i>Pyrogenium</i>	unknown	Mortality	Neg.		19,20
Murine Leukemia Virus (MuLV)	2	MuLV (nosode), DNA, RNA, Prostaglandin	6–200K, 5–15c	Weight of spleen, mortality	Pos.	Spontaneous infection. ¹¹ Preliminary data. ⁴⁶ No potencies, ⁴⁶ only very high dilutions, for treatment and preparation of nosode	11,46

n = number of experiments.

* If not stated otherwise, experiments were performed *in vivo* and infections were induced.

** Some references contained more than one experiment.

Table 3 Summary of infection experiments in chickens

Pathogen	n	Therapeutic substances	Potency range	Observed parameters	Result	Remarks*	Reference**
Chicken embryo virus	3	<i>Typhoidinum</i> , <i>Medorrhinum</i> (<i>Med.</i>), <i>Lyssinum</i> (<i>Lyss.</i>), <i>Anthracinum</i> (<i>Anthraci.</i>), <i>Tuberculinum</i> (<i>Tub.</i>), <i>Nux vomica</i> (<i>Nuxv.</i>), <i>Malandrinum</i> , <i>Acon.</i> , <i>Eup-per.</i> , (<i>Parot.</i>), <i>Agaricus muscaris</i> (<i>Agar.</i>), <i>Pyrogenium</i> , <i>Thuja occidentalis</i> (<i>Thu.</i>), <i>Psor.</i> , <i>Secale cornutum</i> (<i>Sec.</i>), <i>Diphtherinum</i> (<i>Diph.</i>)	Unknown	Number of viral lesions on chorioallantoic membrane	Pos.	Very high efficiency (up to 100%)	18–20
Avian erythroblastosis virus (strain ES4)	4	Geraniol	5–15c	Mortality	Pos.	Unusual pretreatments of medicines. High variability	21
<i>Escherichia coli</i>	1	<i>E. coli</i> (nosode), <i>Carbo vegetabilis</i> (<i>Carb-v.</i>), <i>Arsenicum album</i> (<i>Ars.</i>), <i>Eriodycton glutii</i> (<i>Erio.</i>), <i>Puls.</i> , <i>Gelsemium</i> (<i>Gels.</i>), <i>Ipecacuanha</i> (<i>Ip.</i>), <i>Phosphorus</i> (<i>Phos.</i>), <i>Antimonium tartaricum</i> (<i>Ant-t.</i>), <i>Ferrum phosphoricum</i> (<i>Ferr-p.</i>), <i>Natrum muriaticum</i> (<i>Nat-m.</i>)	30c and 200c	Mortality, weight gain and colibacillosis	Neg.	Similia principle. High-quality study design and statistical evaluation. Simultaneous application of several medicines	17
<i>Salmonella</i> sp.	1	<i>Baptisia tinctora</i> (<i>Bapt.</i>)	30c	Mortality	Pos.	Similia principle. Spontaneous infection	16

n = number of experiments.

* If not stated otherwise, infections were induced.

** Some references contained more than one experiment.

medicines selected according to the similia principle in the treatment of colibacillosis¹⁷ (no positive result).

A large set of medicines was tested for the treatment of chicken's embryo virus in three experiments and strongly positive results were reported (up to 100% efficacy).¹⁸⁻²⁰ Geraniol has shown high efficacy (up to 84%) in the treatment of avian erythroblastosis virus (strain ES4).²¹ Interestingly, the authors investigated various kinds of pre-treatments of the medicines (e.g. heating, distillation) and compared the efficacy.²¹

In contrast to chickens and mice, four of five experiments with dogs utilise cultured canine kidney cells (Madin-Darby Canine Kidney, MDCK cells; see Tables 1 and 6) rather than intact dogs as host organisms. In one experiment with intact dogs, naturally infected animals (heartworm disease) have successfully been treated with *Artemisia nilagirica* (up to 80% reduction of microfilarial titer). But only a few dogs were investigated and there was no control group.²² The remedy was selected after repertorisation. For better comparison, the antiviral activity of several homeopathic complexes against virus-infected cell lines is summarised in the section. Experiments with infected cell lines (see below).

The remaining five animal experiments employed rabbits (1),²³ sheep (1),²⁴ cows²⁵ (1) and guinea pigs (2).^{26,27} Follicle-stimulating hormone, *Cina*, *Phytolacca*, *Calcarea carbonica*, *Silicea*, *Lachesis mutus* and *Variol* (nosode) were investigated, mostly in the treatment of bacterial infections. Three experiments reported positive results^{23,25,27} (Table 4).

Experiments with infected cell lines

Fifteen experiments with infected human ($n = 8$) and animal cell lines ($n = 7$) were published in seven publications^{15,28-33} (Tables 1, 5 and 6). In all but one experiment,¹⁵ the causative pathogen was viral. Antiviral medicines were tested against influenza A virus, human respiratory syncytial virus (RSV), herpes simplex virus 1 (HSV), human rhinovirus type 14 (HRV), adenovirus, human parainfluenza virus 3 and coxsackie virus (Tables 5 and 6). Viral activity was estimated based on plaque reduction, infectious dose of tissue culture, hemagglutination test, transcription of human and viral proteins, virus replication and survivability or morphology of host cells (cytopathogenic effects analysed by light microscopy). Influenza A virus was most resistant to treatments (only one of four medicines was effective [Gripp-Heel[®]; Tables 6 and 7]³¹). In contrast, RSV, and HSV were sensitive to various medicines (Table 5). In two experiments, nosodes were tested (Tables 5 and 6).^{15,32}

The *in vitro* studies primarily investigated the efficacy of homeopathic complexes (Tables 5 and 6). The components of the homeopathic complexes used are listed in Table 7. The homeopathic complexes mainly show moderate effects in the reduction of viral activity (about 20-40%) *in vitro*, but Engystol[®] suppresses viral activity in human Hep-2 cells infected with HSV and adenovirus by up to 80% and 70%, respectively. Interestingly, the authors have

Table 4 Summary of infection experiments in intact dog, rabbit, sheep, cow and guinea pig

Pathogen	n	Therapeutic substances	Potency range	Observed parameters	Result	Remarks*	Reference
<i>Dirofilaria immitis</i>	1	<i>Artemisia nilagirica</i>	200c, 1000c	Number of larvae in blood	Pos.	Dogs. Similia principle. Spontaneous infection	22
<i>Escherichia coli</i>	1	Follicle-stimulating hormone	9c	Overall condition, clinical symptoms, bacterial titer	Pos.	Rabbit	23
Various digestive tract nematodes	1	<i>Cina</i>	9c, 15c	Reduction of nematodal eggs	Neg.	Sheep. Similia principle. Spontaneous and induced infections	24
<i>Staphylococcus aureus</i>	1	<i>Phyt.</i> , <i>Calc.</i> , <i>Sil.</i>	6c	Mastitis-test, reduction of bacterial cells	Pos.	Cow. Similia principle	25
<i>Vaccinia virus</i>	1	<i>Vario.</i>	200d	Severity and duration of clinical symptoms	Pos.	Guinea pig. Similia principle. Not isopathy, because nosode was made from different pathogen	27
<i>Clostridium</i> sp.	1	<i>Lach.</i>	8d	Mortality	Neg.	Guinea pig	26

n = number of experiments.

* If not stated otherwise, infections were induced.

Table 5 Summary of infection experiments in human cell lines

Cell line	n	Pathogen	Therapeutic substances	Observed parameters	Result	Reference*
Hep-2	4	Human respiratory syncytial virus (RSV)	ECS, ECSN, <i>Euph.</i> (D3), <i>Puls.</i> (D3), Engystol [®] , Gripp-Heel [®] (see Table 7)	Plaque reduction, estimation of tissue culture infectious dose, transcription of viral proteins	Pos.	28–31
Hep-2		RSV	<i>Luf-op.</i> (D4)	Plaque reduction	Neg.	29
Hep-2		Herpes simplex virus 1	ECS, ECSN, Engystol [®] , Gripp-Heel [®] (see Table 7)	Plaque reduction, transcription of viral proteins, estimation of tissue culture infectious dose	Pos.	28–31
Hep-2		Human parainfluenza virus	Gripp-Heel [®] (see Table 7)	Plaque reduction	Pos.	31
Hep-2		Adenovirus	Engystol [®] , Gripp-Heel [®] (see Table 7)	Transcription of viral proteins, estimation of tissue culture infectious dose, cytopathogenic effects	Pos.	30,31
HeLa	4	Human rhinovirus type 14 (HRV-14)	Engystol [®] , Gripp-Heel [®] (see Table 7)	Plaque reduction, estimation of tissue culture infectious dose	Pos.	30,31
HeLa		HRV-14	ECSN (see Table 7)	Plaque reduction	Neg.	29
HeLa		Adenovirus	Adenovirus (nosode)	Transcription of specific human protein	Pos.	32

n = number of experiments.

* Some references contained more than one experiment.

also started to investigate the mode of the direct antiviral action (as distinguished from the known immunomodulating effects^{34–39}) of these homeopathic complexes,^{30,31} but this kind of research is still in its infancy.

For the sake of clarity, all experiments applying animal cell lines (mice, dogs, monkeys) are summarised separately in Table 6. Human cell line research is summarised in Table 5.

Discussion

Several publications report positive results when homeopathic medicines are used to treat infected organisms or cell lines. Unfortunately, to date no medicine has been tested twice in the same organism/cell line and no independent reproduction of any experiment was reported. Therefore, no immediate information is available from basic research experiments concerning medicines to be tested in clinical trials. In addition, more than half of the experiments are flawed in some manner (e.g. high variability of data, low statistical power, incomplete data and undefined potency). Even if no immediate stimulus for clinical trials can be deduced at the moment, some subtle information arises and some general conclusions can be drawn from the presented studies.

The similia principle

The similia principle is the central therapeutic tenet in homeopathy. Normally, the *similimum* is found using a rep-

ertory. However, information on animal drug provings⁴⁰ and information on veterinary *Materia medica*⁴¹ are sparse (not to mention the situation of *in vitro* experiments applying human or animal cell lines). Therefore, medicines are usually chosen after consultation with a human repertory as the best available solution. However, the transferability of a human repertory to animal disease symptoms is doubted by several authors.^{42,43}

Nevertheless, we investigated on what basis of assessment medicines were chosen in the reported infection experiments. In contrast to our expectation, only in eight experiments medicines were selected according to the similia principle after consultation with a *Materia medica* or repertorisation.^{12,13,16,17,22,24,25,27} Six of these (75%) had positive results (Tables 2–4).^{12,13,16,22,25,27} These results support the validity of the core principle of homeopathy and should guide researchers in further basic and clinical research. In addition, of eight^{12,15,17,27,32,44,45} experiments with nosodes directly prepared from the causative pathogen or prepared from tissue infected with the pathogen under investigation (isopathy),⁴⁶ again six (75%) were positive.^{12,15,32,44–46}

Homeopathic pathogenetic trials of homeopathic complexes have not been done and hence the application of homeopathic complexes cannot be based on the similia principle. In addition, most homeopathic complexes utilised in homeopathy basic research, reviewed here, are

Table 6 Summary of infection experiments in animal cell lines (various species)

Host cell origin	n	Pathogen	Therapeutic substances	Cell line	Observed parameters	Result	Reference
Mice	1	<i>Leishmania braziliensis</i>	<i>L. braziliensis</i> (nosode)	Macrophages	Survival of amastigotes	Neg.	15
Dog	3	Influenza A	Various homeopathic complexes (see Table 7): Engystol [®] , ECS, ECSN Gripp-Heel [®] (see Table 7)	MDCK	Plaque reduction, estimation of tissue culture infectious dose, hemagglutination assay	Neg.	28–30
Monkey	1	Coxsackie virus B4	Complex drug (see Table 7)	Monkey kidney cells	Virus replication	Pos.	31
Monkey	1	Coxsackie virus A9	Gripp-Heel [®] (see Table 7)	Buffalo Green Monkey kidney cells	Plaque reduction	Neg.	33
						Pos.	31

n = number of experiments.

Table 7 Composition of homeopathic complexes

Trade name	Ingredients
Gripp-Heel® ECSN	Acon., Bry., Eup-per., Lach., Phos. Euph., Puls., <i>Luffa operculata</i> (Luf-op.), <i>Mercurius iodatum rubrum</i> (Merc-i-r.), <i>Hepar sulphuris</i> (Hep.), <i>Argentum nitricum</i> (Arg-n.)
ECS	<i>Euphrasia</i> (Euph.), Puls., Luf-op., Merc-i-r., Hep., Arg-n., <i>Mucosa nasalis suis</i> , <i>Sinusitis-nosode</i>
Engystol® Complex drug*	<i>Vincetoxicum hirundinaria</i> , Sulphur (Sulph.) <i>Cactus grandiflora</i> (Cact.), <i>Aloe socotrina</i> , (<i>IAbies-n.</i>), <i>Arnica montana</i> (Arn.), Lach., Calc., <i>Lycopodium clavatum</i> (Lyc)

* Drug described by See *et al.*³³

based not on homeopathy but on homotoxicology. However, homeopathic complexes and homotoxicology are related to homeopathy in certain aspects and therefore were included in the HomBRex database and in this review.

Repetitions

Only four substances were tested in more than two experiments (but with different hosts or pathogens): *Eup-per.*, *Lach.*, *Cina* and *Puls.* *Eup-per.* were tested with nine viruses. As a component of the complex drug Gripp-Heel®, *Eup-per.* demonstrated moderate antiviral activity in human and animal cell lines.³¹ However, it is impossible to discriminate whether *Eup-per.* contributed to the antiviral activity or not. Two other experiments demonstrated no²⁰ or high¹⁸ antiviral activity. In the one remaining experiment, *Eup-per.* expressed high activity (60–70%) with the protozoon *Plasmodium berghei*.¹³ *Lach.* was tested with two types of bacteria (*Clostridium septicum* and *C. novyi*) with negative results; contrary results were reported regarding the antiviral activity in monkey cell lines and mice infected with different strains of coxsackie virus (*Lach.* as a component of homeopathic complexes).^{31,33} *Puls.* was tested *in vitro* as part of a complex drug and as a sole treatment in various antiviral assays with positive and negative results.^{28,29} No antibacterial activity was found.¹⁷ Finally, *Cina* and its close relative *A. nilagirica* were tested against various types of nematodes in mice, dogs and sheep, again with contradictory results.^{14,22,24}

In summary, it is difficult to find general tendencies with the given low number of experiments. An aggravating factor is that different hosts were employed and the anti-pathogenic activity was based on different observables by the various authors. No general antiviral, anti-parasitic or antibacterial activity of any of the more frequently tested substances can be deduced at this point.

In vitro vs. in vivo

At first glance, *in vitro* basic research with infected cell lines seems to be a valuable tool for testing anti-pathogenic characteristics of homeopathic medicines. This is suggested by the encouraging experiments with various human, dog and monkey cell lines that gain support from respective clinical studies: clinical trials and case series have demonstrated

the effectiveness of Gripp-Heel[®], Engystol[®] and Euphorbium Compositum[®] in viral infections,^{36,47–57} and there is a solid base for the use of these homeopathic complexes in respiratory tract infections. On the other hand, contradicting results were reported: Engystol[®] has demonstrated direct antiviral activity in human cell lines with RSV and reduced the number of plaques by 40% and the infectious dose by 20%.³⁰ However, the clinical trial suggests only positive immunostimulating effects of Engystol[®] and no direct antiviral action, because the elimination of the RSV-antigen is not enhanced.

The nosode of *Leishmania braziliensis* does not reduce the survivability of amastigotes of this pathogen in mouse macrophages but does reduce the diameter of the lesions in intact mice¹⁵ and the complex drug described by See *et al.*³³ reduces the virus-titer in mice by 30% but fails to inhibit the replication of the virus *in vitro*. Admittedly, different forms of the pathogen (amastigotes ↔ promastigotes) or different host organisms (mice ↔ monkey kidney cells) were investigated in the last two studies.^{15,33}

This might be the cause of the varying effectiveness. Other reasons might be the different bioavailability of the medicines in cells and intact organisms or the absence of all components of the immune system in isolated cells under the assumptions that the specific action of homeopathic medicines is based on the interaction of homeopathic preparations and the immune system (which is still to be proven). The transferability of *in vitro* results to intact organisms is not generally given in conventional medicine either, and it has to be established for every single model and active agent. In conclusion, the transferability of *in vitro* results with homeopathic medicines to intact organisms needs further substantiation.

Counterproductive effects in homeopathic complexes?

Special attention is turned to Euphorbium compositum S[®] (ECS) and Euphorbium compositum SN[®] (ECSN). Both homeopathic complexes share almost identical ingredients (Table 7) but express somewhat different antiviral activity. Both are ineffective in the treatment of influenza A infected canine cells but reduce the number of viral plaques caused by RSV by up to 35% (ECS) or 40% (ECSN). In addition, ECSN inhibits the activity of HSV by up to 40%, whereas plaques are only reduced by 30% after treatment of infected Hep-2 cells with ECS. Strangely, the complex with additional ingredients demonstrates diminished efficacy.

Whether this difference is due to counterproductive effects by the additional components in ECS (*Mucosa nasalis suis*, *Sinusitis-nosode*) or due to the standard deviation of about 10%, might be interesting to explore. Glatthaar-Saalmüller and Fallier-Becker suggest *Euph.* and *Puls.* to be the main active components with regard to the antiviral action (isolated *Luf-op.* was shown to be ineffective)²⁹ in ECSN. However, the other non-plant-derived ingredients of ECSN have not been examined in extra experiments and additional antiviral effects, based on the interplay of the ingredients with each other, cannot be ruled out.

Conclusion

It can be finally concluded that many different medicines have proven effective in single basic research experiments for the treatment of infected organisms and cell lines. However, all experiments await replication and no clear-cut conclusion can be drawn regarding the similia principle, the transferability of *in vitro* results to *in vivo* outcomes and new stimuli for clinical research, at the moment. Additional information might appear from *in vitro* experiments where homeopathic medicines were tested directly against bacteria, fungi, proto-/metazoa without any host organisms. These types of experiments were excluded in the present work but will be the subject of a forthcoming review.

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