lengths: our results show that the complexity and symmetry of polycrystalline structures correlates with the viability of non-stressed and stressed wheat seeds following *Arsenicum album* HD with respect to control.

These first results indicate that the droplet evaporation method might constitute a support for experimental trials and/or a pre-screening method for treatment test, since it shows to be sensitive to the sample vitality.

Keywords: Droplet evaporation method, Polycrystalline structures, Bilateral symmetry, Fractal dimension, Arsenic trioxide, Ultra high dilutions

Model validity of randomised placebo-controlled trials of individualised homeopathic treatment

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Purpose: A new programme of systematic reviews of randomised controlled trials (RCTs) of homeopathy distinguishes several key attributes of study design and quality: placebo controlled *cf.* other-than-placebo controlled; individualised *cf.* non-individualised homeopathy; treatment *cf.* prophylaxis; internal validity *cf.* model validity. The present phase of the review programme focuses on assessing the model validity (MV) of peer-reviewed, placebo-controlled, RCTs of individualised homeopathic treatment.

Methods: A systematic literature search and subsequent reappraisal of retrieved records identified 31 RCTs that satisfied the inclusion criteria for the present study. MV of the eligible RCTs was appraised using a novel criterion-based method. Assessment domains address: (i) the rationale for the choice of the particular homeopathic intervention; (ii) the homeopathic principles reflected in the intervention; (iii) the extent of homeopathic practitioner input; (iv) the relevance of the main outcome measure; (v) the capability of the main outcome measure to detect change; (vi) the length of follow-up to the endpoint of the study. These six MV domains per RCT were categorised by each of three independent assessors as 'acceptable', 'unclear' or 'unacceptable', disparities of opinion being resolved by consensus discussion.

Results: Domain-specific and overall ratings of MV per RCT await the outcome of ongoing consensus discussions. A full set of findings will be presented at conference.

Conclusions: MV data contribute importantly to the appraisal of RCT quality in systematic reviews of homeopathy.

Study of Gelsemium sempervirens in a neurocyte model. An update

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Previous investigations showed significant anxiolytic-like activities of *Gelsemium sempervirens L.* (*Gelsemium s.*) in mice models. To provide new insights into the neural substrates of anxiety and to identify drug targets, we decided to investigate the *Gelsemium s.* mechanism of action in neuronal models by assessing the genome expression changes. The SH-SY5Y and IMR-32 human neuroblastoma cells were used since are widely employed in neuropharmacology and well characterized. The drugs were produced by Boiron Laboratoires (Lyon), starting from a whole-plant-hydroalcoholic extract and the cells were treated with 6 increasing dilutions 2c, 3c, 4c, 5c, 9c, 30c. We compared the drug effects with those of control solutions prepared by the same procedure, but with the solvent vehicle without the plant extract. All dilution steps were followed by strong succussion. Final ethanol concentration was 0.03% v/v. After having ruled out possible toxic effects of any test solution on cell viability, we evaluated gene expression firstly by using a microarray designed for the whole human transcriptome (Nimblegen, Roche). We used the Limma statistics approach (n=4 biological replicates) to select a set of differentially expressed genes and Friedman test followed by Wilcoxon signed-rank test to check the null hypothesis that high dilutions have no effect in this model. The exposure to 2c dilution promoted a small (fold changes between 0.5 and 1.0) but significant down expression of 49 genes as compared with untreated controls. With higher dilutions, most of the genes down-regulated in the 2c-treated samples were also under-expressed in 3c and, to a varying extent, even in higher dilutions. No changes of housekeeping genes were recorded, confirming the specificity of drug action. The changes in the 49 selected genes of SH-SY5Y cells were in the same direction in the IMR32 cells, showing that the expression of the same gene set was also modified in a second type of neurocyte. Afterword we performed the RT-qPCR on a subgroup of relevant genes modulated in 2c treatment (i.e. transcription factors, G-protein coupled receptors or neuropeptides) and we confirmed the down-regulation for the genes DDI1, EN2, GALR2, GPR25, OR5C1, Klkbl4 and TAC4. In the Wilcoxon analysis, applied to the 49 genes, the number of down-regulated ones was systematically higher than the number of genes with positive fold change over all dilutions ($p<0.0001$). No significant differences between treatments and controls in a randomly chosen gene set of 49 genes were observed, suggesting that the *Gelsemium s.* effects are not due to chance. In parallel we

adopted, for the dilutions 2c and 9c, an RT-PCR Array approach (SABioscience, Qiagen) containing 84 genes, including receptors and regulators of neuronal function. In this further investigation we observed a trend to down-regulation for DRD2, CHRN4B, CHRNG, PROKR2 and PHOX2A genes in 2c and BRS3, GRPR genes in 9c dilution. In particular the down-regulation of DRD2 and PROKR2, effective in the inhibition of Gabaergic neurotransmission, suggests a specific effect of *Gelsemium s*. in increasing the endogenous GABA activity. Overall, the genes modulated in this experimental model outline new working hypotheses on the anxiolytic and analgesic action of this plant. In conclusion this study provides evidence that *Gelsemium s*. exerts a prevalently inhibitory effect on a series of genes, in particular involved in G-protein coupled transduction systems, in olfactory transduction, in calcium signaling and in neurotransmission. Furthermore the whole genome expression analysis (microarray and real-time PCR), indicates that the "omics" molecular biology is a suitable approach to study the effects of highly diluted natural compounds.

In-vitro experiments to investigate the effects of homeopathic drugs for chronic aggressive periodontitis by lymphocyte migration activity

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Background: Several homeopathic drugs are applied in the treatment of periodontal inflammation. However less is know about the basic working principles of highly diluted remedies in such chronic inflammatory conditions. We therefore aimed at investigating the effects of homeopathic drugs in periodontal inflammation by observing lymphocyte migration activity.

Material and Methods: Lymphocytes from blood samples of three patients suffering on chronic aggressive periodontitis and three matched healthy volunteers were extracted and enbedded in a collage matrix migration assays together with highly diluted (D12 and C200) aquaetous extract from Mercurius solubilis, Silicea, Sulfur, Tuberculinum, or placebo. Activity and speed of lyphocytes were observed in a 60 min time frame using flow cytometry. Statistical analysis was performed using univariate statistics and SiZer time series analysis.

Results: A significantly reduced migration activity and speed was observed in lymphocytes extracted from the patients suffering on chronic aggressive periodontitis compared to those of healthy volunteers (mean activity: 12.5% vs. 26.3%). While C-potencies did not reveal strong differences between placebo and substances some meaningful effects were observed in D-potencies compared with placebo: moderate but not significant inhibiting effects with regards to activity were observed in lymphocytes treated with Silicea extract (mean activity: 13.3% vs. 11.9% in patients' and 26.2% vs. 22.2% in healthy samples). The strongest and most specific effects were observed in Sulphur D12 which showed an activating effect in lymphocytes of patients (mean activity: 11,1% vs. 23,8%) but not in those of healthy volunteers (25,8% vs. 25,6%). SiZer analysis confirmed this effect to be significant.

Conclusion: Discussion about the basic working principles of highly diluted substances is still vital and leads to controversies in the scientific discussion. Although conclusions are limited due to low sample size, our pilot study was able to reproduce former results on lymphocyte migration activity and thus proves model validity. Results from our pilot study might encourage further investigations on the role of highly diluted Sulphur in the treatment of periodontitis.

Use of homeopathy for prophylaxis of urinary tract infections in patients with neurogenic bladder dysfunction

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Background: Patients with neurogenic bladder dysfunction are prone to various urologic disorders which sometimes cannot be appropriately treated. Especially recurrent urinary tract infections (UTI) in patients with spinal cord injury are a frequent clinical problem. Often, conventional preventive measures are not successful. We present our initial results of collaboration between homeopaths and urologists in these patients.

Materials and Methods: after exclusion of morphologic abnormalities and initiation of a standard regime for prophylaxis, all patients with a neurogenic lower urinary tract dysfunction (NLUTD) due to spinal cord injury (SCI) with more than 3 symptomatic UTI/year were offered additional homeopathic care (classical homeopathy with an individualized approach). UTI symptoms were fever, incontinence, increased spasticity, decreased bladder capacity or pain/