

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. Afterward 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, Kikbl4 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