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Scientific criticism in homoeopathy: need to test more than disputes

To the Editor:

We have been following the debate in this journal on homoeopathy, its adverse effects and related technical issues. We are not homoeopaths, but university researchers interested in this field, and we intend to briefly discuss some aspects of how homoeopathy is considered and specifically of our studies on homoeopathic dilutions of *Gelsemium*. In the September 2013 issue, Chirumbolo wrote a lengthy letter (1) intended to 'provide some explanation of the strange way by which homeopaths participate in whatsoever is coming up from a scientific debate'. There, he also maintains that 'there are people who are not inclined to discuss fairly about their research work. And yet homoeopaths are going ahead on their ideological struggle'. Yet, he fails to provide any clear evidence of the facts that might back up these prejudicial and unsubstantiated statements. The letter includes several citations and criticisms of our papers on *Gelsemium sempervirens* (2,3), and casts certain aspersions on the correctness of our ethical position. Chirumbolo in his letter cites the case of his paper, which was rejected by Frontiers in Neurology purporting that this was because of incorrect actions by one of us, but this absurd suspicion is not supported by any evidence. The same author then cites the case of a debate with Dr. Cervo and Torri, maintaining that 'an Author from the discussed paper (2) ridiculed their legitimate attempt to give a response, by showing their rejected letter in a slide during an International Congress in Brazil etc.' This declaration is simply false as the mentioned slide was not shown. The author argues that previous debates on *G. sempervirens* as an anxiolytic compound 'elicited neither any serious revision, nor a point-by-point reply to the addressed issues'. This is simply untrue. Readers will be well aware that this is the fourth opinion letter from that same author criticising our work (1,4–6), but no experimental proof invalidating our published experimental findings was produced. In point of fact, all the theoretical criticisms raised – except for those which are manifestly unfounded – have been discussed and clarified in various replies and in a series of scientific papers (7–10). Contrary to what the cited letter asserts (1), the concerns relating to the applications of anxiety models in homoeopathic research have been thoroughly addressed and an unbiased perusal of them should be enough to confirm the validity of our findings and interpretations. Chirumbolo then reiterates some critical points concerning statistics and interpretations raised by another commentary (11), to which we have already extensively responded (7,12). Then he maintains that 'when most homeopaths are invited to any civil and polite match, prejudices appear to overwhelm any good debate' and 'homeopaths have the purpose to hamper any good revision'. We wonder whether this and other similar sentences can be considered as 'scientific criticism'. Regarding the purported toxicity of homoeopathic medicines and the risk of adverse effects, the author forgets to say that homoeopathic remedies – according to the U.S., European and Italian pharmacopoeias and legislation – are used in dilutions such that they cannot have direct toxic effects. Moreover, adverse effects of homoeopathic drugs are exceedingly rare and these therapies are well tolerated (13,14). We have demonstrated with placebo-controlled studies in behavioural models that the dilutions 5c, 7c, 9c and 30c of *G. sempervirens* (2,3) and of *Ignatia amara* (15) have anxiolytic-like properties without weakening locomotion and without adverse or sedative effects. As a matter of fact, the anxiolytic power of *Gelsemium* alkaloids has been recently confirmed by other laboratories (16–18). Table 1 summarises the main evidence and relevant discussed points in this debate. We hope that these clarifications are welcomed in the interests of providing correct and truthful information to readers. Basic research in homoeopathy is a new field that is fascinating, but challenging,

Table 1 Evidence and interpretations of the Gelsemium effects in laboratory models

Issue	Evidence and/or interpretation	References
Validity of test models	Experiments were performed using ethologically based paradigms that involve spontaneous reactions to non-painful stimuli. Open-field and light-dark are among the most validated behavioural paradigms in rodents. Tests were carried out on randomised mice and group treatments were carried out in blind	(2,19–22)
Validity of statistical tests	ANOVA was used correctly as data distribution was normal, groups had similar variability and the power of the study was correctly computed	(2,8,12)
Ethanol in test solutions	Final ethanol concentration in test drugs was 0.3%, which does not interfere with mice behaviour and in any case, the same dose is present in control (placebo) solutions	(8,9,23)
Toxicity of gelsemine	Homoeopathic treatments were accomplished through the administration of extremely low doses (less than 10^{-12} mol/l) that are absolutely non-toxic	(2,8)
Replicability in the same laboratory	Two subsequent series of experiments testing Gelsemium in similar experimental setting showed the anxiolytic-like effect, with some quantitative differences according to test employed. A pooled data analysis confirmed this effect	(2,3,9)
Findings from other laboratories	The anxiolytic-like effect of Gelsemium or of its active principle gelsemine was recently reported by several other laboratories	(17,18,24,25)
Lack of dose–response	The majority of works testing different dilutions/dynamisations in a variety of plant, cellular and animal models report non-linear patterns and even multiple peaks of activity and so on. Data that do not fall into a linear dose–response relationship are not at all uncommon in pharmacology and occur for a host of possible reasons (see hormetic effects and nanoparticles)	(26–31)
Plausibility	Similia principle is plausible and rationale in several fields of medical science. Gelsemium alkaloids are neurotoxic at high doses and therapeutic at low doses	(32–34)
Hypothesis on the mechanism of action	Gelsemium s. dilutions affect neurosteroid biosynthesis and modulate gene expression in neuronal cells	(16,29,35)

because it deals with the difficult-to-solve technical issues of high dilutions, hormesis and paradoxical reversal of the effects of drugs. One would therefore expect the related questions to be addressed not through subjective opinions and jeering, but rather on the experiential ground, through patient and critical comparison of data and results.

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Disclosure

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LETTER

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Short-term mortality in acute coronary syndrome: effect of dysglycaemia and smoking

To the Editor:
Coronary artery disease (CAD) is a major cause of morbidity and mortality burden in the developing world, including India (1). There is growing evidence that dysglycaemia, irrespective of the history of diabetes, is associated with adverse outcomes in coronary artery bypass graft surgery patients (2–4).

Diabetes mellitus or impaired glucose tolerance, smoking or tobacco use in any form, not only predisposes to development of acute coronary syndrome (ACS) but also affects the