Nanomaterial Characterisation of Diluted *Platina* and Alcohol Control Samples

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Abstract

Background The healing effects of homeopathic ultra-high potencies (UHPs) have always been a puzzle for material science, though recent research papers have now characterised the nanomaterial nature of several such UHPs. This study aimed to analyse the material content of clinically used potencies of the homeopathic medicine *Platina* (platinum) compared with alcohol control samples.

Methods Potencies of *Platina* were analysed under dynamic light scattering (DLS), high resolution transmission electron microscopy (HRTEM) with energy dispersive spectroscopy (EDS) and selected area electron diffraction (SAED) to identify the nanomaterial content. As control samples, both unsuccussed and potencies of alcohol were analysed by using DLS and HRTEM.

Results *Platina* 30c to CM: Nanoparticles were identified under DLS (mean particle size varying from 1.3 nm in 30c to 6.5 nm in CM) and HRTEM (particle size varying from 3.31 to 12.7 nm in 30c to 1.94 to 8.54 nm in CM). EDS confirmed the presence of platinum in all the samples of *Platina*. SAED analysis of *Platina* 30c, 200c, 1M and 10M confirmed also the presence of platinum dioxide (PtO_2). For control samples, DLS and the HRTEM analyses of pharmaceutical grade unsuccussed alcohol and potentized *Alcohol* (6c, 12c and 30c) did not show any particles.

Conclusion Homeopathic potentization generated NPs of platinum in ultra-dilutions. NPs in potencies of *Platina* showed platinum in EDS and PtO_2 in SAED. Importantly, control samples of alcohol did not show the presence of particles under DLS or HRTEM.

Keywords
- nanoparticles
- nanopharmacology
- ultra-high potencies
- *Platina*

Introduction

Homeopathic ultra-high potencies (UHPs) have been used by homeopathic physicians around the world for the last two centuries in the treatment of multiple different illnesses. Using modern technology, the outcome of recent research provides ample evidence of the fact that UHPs of homeopathy contain nanoparticles (NPs) of source material.[1–10]

In historical debates during the many decades of this discipline, plausibility arguments and experimental evidence[11] have supported new and incoming perspectives,[12] and these clearly favoured the nanoparticulate nature of homeopathic UHPs. This idea was furthered by some to view homeopathy as unique and personalised nanomedicine,[10] opening the possibility for further exploration into homeopathy and its therapeutics based on UHPs.

The sample medicines used for the current study and the control samples of alcohol potencies were prepared according to the guidance of the Homeopathic Pharmacopoeia of India (HPI).[13] The manufacturing process of homeopathic UHPs involves step-by-step dilution and potentization, not simple dilution alone. Recent developments show that the manufacturing process of homeopathic potencies is similar to the top-down approach being adopted in nanotechnology,[14] giving additional insight into the whole process of homeopathic medicine preparation and its nanopharmacology.

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In the majority of the studies of homeopathic UHPs, the sample potencies being studied have been in the range of 200c.[1,3] The present study has been designed for the analyses of various sample potencies of *Platina* (30c to CM) and comparison with sample potencies of alcohol as control.

Platina is a homeopathic constitutional medicine proved by Dr. Samuel Hahnemann and described in his book 'Chronic Diseases'.[15] In clinical practice, *Platina* is prescribed for conditions such as depression, delusions and hysteria, and for uterine, ovarian and autoimmune disorders.[16]

Materials and Methods

Samples

The samples of *Platina* were procured from Willmar Schwabe India (P) Ltd., New Delhi, a GMP-certified ISO 9001:2015 homeopathic pharmaceutical company.

The glassware used in the preparation of UHPs was pharmaceutical grade USP type III soda-lime-silica glass. In the preparation of potencies, separate glassware was used up to 200c. From 200c to CM potency, the same glassware was used in the mechanized potentizer, giving 10 succussions (vertical agitations) in every step. Pharmaceutical-grade alcohol, as per the HPI, was used as a vehicle for the preparation of all UHPs. The same pharmaceutical-grade alcohol was procured from Willmar Schwabe India (P) Ltd., New Delhi, for the preparation of alcohol control samples. Sterile, pharmaceutical grade soda-lime-silica glassware was used for the preparation of control samples. The control samples were prepared according to the existing method of preparation of centesimal scale of potencies as described in the HPI.[13] Potencies were prepared at the ratio of 1:99 of the previous potency to the vehicle. Ten powerful downward strokes on a hard, elastic body were applied for the preparation of potencies. Separate glassware was used for the preparation of control samples of alcohol.

Instruments

Dynamic light scattering (DLS) analysis was conducted with Horiba scientific nanopartica SZ-100, path length 100 nm. It helped to analyse the NPs and find their average size.

High resolution transmission electron microscopy (HRTEM) was conducted in a Jeol TEM 2100 with an operating voltage 200 kV; a 200-mesh carbon-coated copper grid was used for the analysis of the sample. The energy dispersive spectroscopy (EDS) analyses were performed with an Oxford instrument INCA, which helped to analyse the elemental composition of the NPs. The HRTEM and the EDS analyses were performed simultaneously. Selected area electron diffraction (SAED) images were captured during the HRTEM analysis.

Preparation of Samples and Analysis

DLS Analysis

1. *DLS analysis of* Platina: The selected samples of UHPs of *Platina* were sonicated for 20 minutes at 50 Hz. Immediately after sonication, 2 mL of the drug solution was taken in a well-cleaned quartz cuvette and mounted into the DLS chamber for analysis.
2. *DLS analysis of alcohol:* The selected samples of pharmaceutical grade unsuccussed alcohol and potentized *Alcohol* were sonicated and analysed, as in the case of *Platina.*

HRTEM and EDS Analyses

1. *HRTEM and EDS analyses of* Platina: Samples of *Platina* were sonicated for 20 minutes at 50 Hz. One micro-drop of the solution was taken from the middle of the bottle with a micro-pipette and dropped on the TEM grid. The grid was dried overnight under an infrared lamp. The grid was mounted on the TEM chamber and the NPs were identified. For *Platina* samples bright-field TEM images were taken and the particle size was measured. SAED images were taken during the TEM analysis. Simultaneously, EDS was used to determine the composition of the NPs.
2. *HRTEM and EDS analyses of alcohol:* The control samples of pharmaceutical grade unsuccussed alcohol and potentised *Alcohol* were sonicated and analysed under HRTEM, as in the case of *Platina.* EDS analysis could not be performed, as no particles were found during the HRTEM analysis.

Results

DLS Analyses of *Platina* and Alcohol Control Samples

The DLS analyses of *Platina* 30c to CM potencies showed the presence of NPs with a mean particle size of 1.3 nm (30c, ►**Fig. 1A**), 5.00 nm (200c), 0.7 nm (1M), 1.7 nm (10M), 6.2 nm (50M) and 6.5 nm (CM) [**Supplementary files: 1.1**—DLS image of *Platina* 30c; **1.2**—DLS image of *Platina* 200c; **1.3**—DLS image of *Platina* 1M; **1.4**—DLS image of *Platina* 10M; **1.5**—DLS image of *Platina* 50M; **1.6**—DLS image of *Platina* CM]. The supplementary files are available online only.

The DLS analyses of pharmaceutical grade unsuccussed alcohol and *Alcohol* 6c, 12c and 30c (►**Fig. 1B**) did not show the presence of any particle [**Supplementary files: 2.1**—DLS image of pharmaceutical grade unsuccussed alcohol; **2.2**—DLS image of *Alcohol* 6c; **2.3**—DLS image of *Alcohol* 12c; **2.4**—DLS image of *Alcohol* 30c]. The supplementary files are available online only.

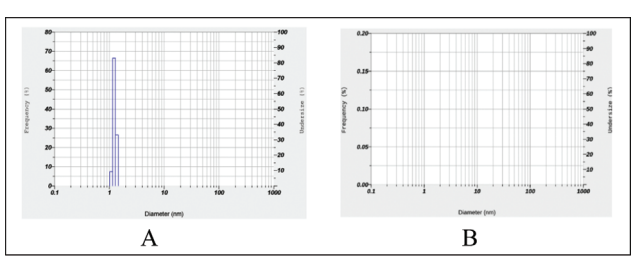

Fig. 1 DLS graph of *Platina* 30c **(A)** and *Alcohol* 30c **(B)**. DLS, dynamic light scattering.

HRTEM and EDS Analyses of *Platina* and Alcohol Control Samples

Platina 30c, 200c, 1M, 10M, 50M and CM potencies were analysed by HRTEM and EDS. The results are given as HRTEM images (►**Figs. 2A** and **B**, **3A** and **B**, **4A** and **B**, **5A** and **B**, **6A** and **B** and **7A** and **B**), which clearly demonstrate the presence of NPs and aggregates. NPs showed polydispersity in relation to their size and shape. The morphology of NPs was different from 30c to CM; moreover polydispersity was noticed within the same potency.

Confirmation of the Elemental Composition of Particles by EDS

EDS analysis was performed and the elemental composition of the particles was identified in all the samples (►**Table 1**). EDS is used to analyse the elemental composition of solid

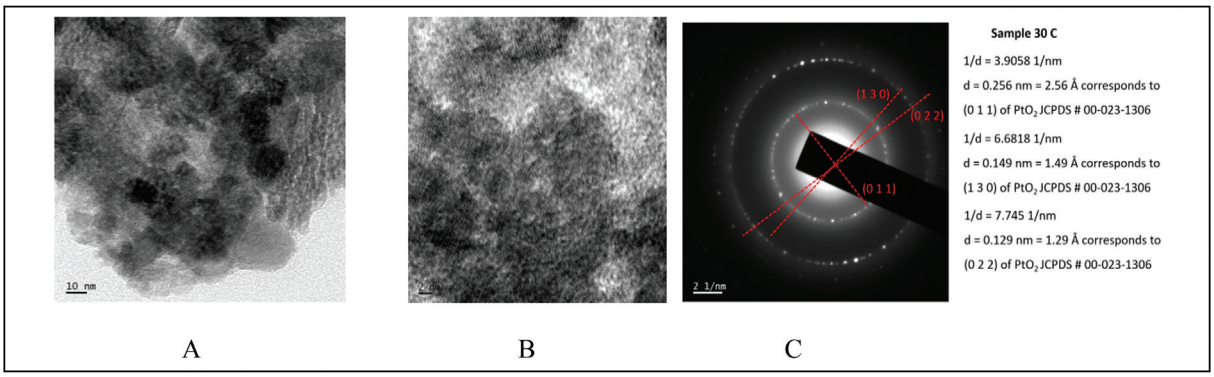

Fig. 2 HRTEM images of *Platina* 30c, scale bar 10 nm **(A)**, 2 nm **(B)**; and SAED **(C)**. HRTEM, high resolution transmission electron microscopy; SAED, selected area electron diffraction.

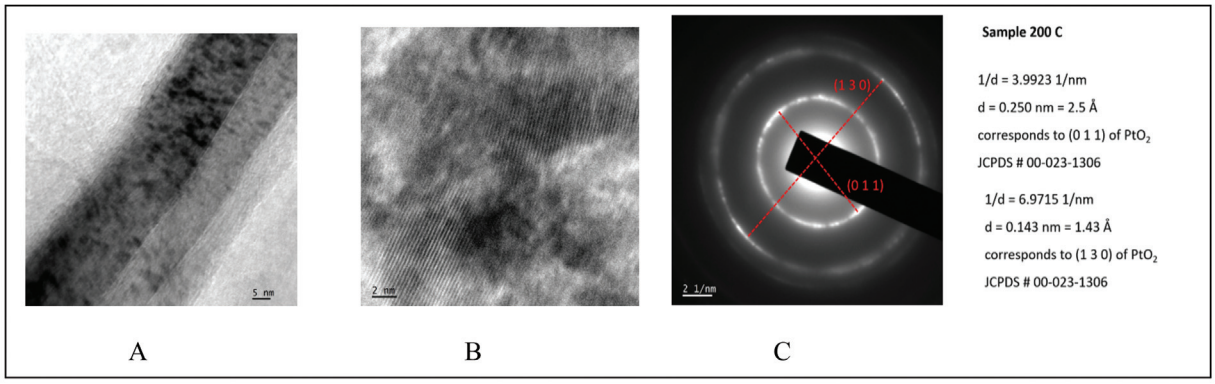

Fig. 3 HRTEM images of *Platina* 200c, scale bar 5 nm **(A)**, 2 nm **(B)**; and SAED **(C)**. HRTEM, high resolution transmission electron microscopy; SAED, selected area electron diffraction.

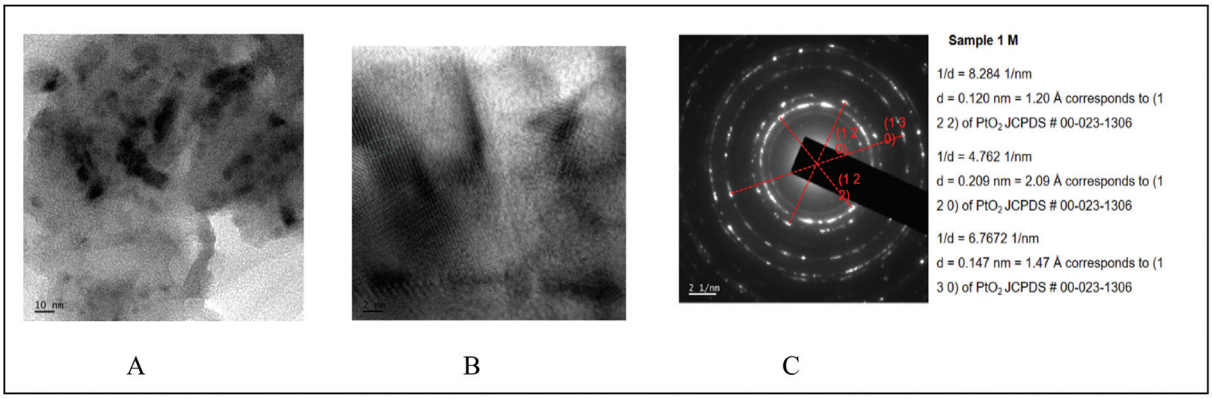

Fig. 4 HRTEM images of *Platina* 1M, scale bar 10 nm **(A)**, 2 nm **(B)**; and SAED **(C)**. HRTEM, high resolution transmission electron microscopy; SAED, selected area electron diffraction.

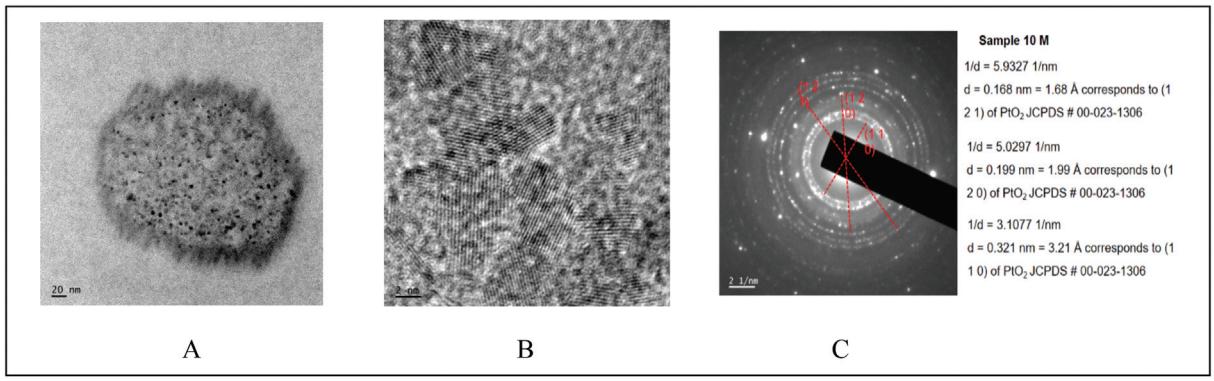

Fig. 5 HRTEM images of *Platina* 10M, scale bar 20 nm **(A)**, 2 nm **(B)**; and SAED **(C)**. HRTEM, high resolution transmission electron microscopy; SAED, selected area electron diffraction.

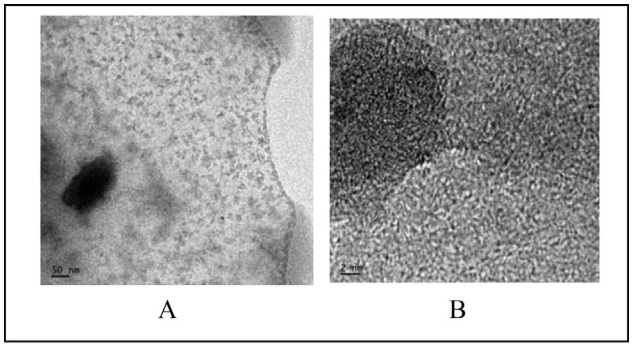

Fig. 6 HRTEM images of *Platina* 50M, scale bar 50 nm **(A)** and 2 nm **(B)**. HRTEM, high resolution transmission electron microscopy.

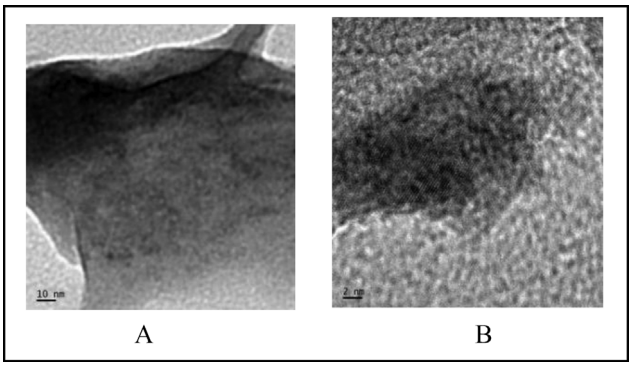

Fig. 7 HRTEM images of *Platina* CM, scale bar 10 nm **(A)** and 2 nm **(B)**. HRTEM, high resolution transmission electron microscopy.

surfaces. During the analysis the X-ray emission is stimulated by irradiation of the surface with a high energy beam of charged particles. Excitation of the electronic structure of an atom can produce an X-ray emission, the energy signature of which is a unique characteristic of each element. Therefore, a signature spectral fingerprint can be obtained, allowing identification of an element via comparison with reference spectra. Platinum (Pt) was detected in all the potencies of *Platina* (**Supplementary files 3.1** to **3.6:** EDS graphs of *Platina* 30c, 200c, 1M, 10M, 50M and CM respectively; available online only).

SAED Analysis Confirmed the Presence of Platinum Dioxide

SAED is a crystallographic experimental technique performed using a transmission electron microscope. In SAED, standard crystallographic diffraction patterns are used to identify the material. In a SAED pattern, the spots are due to the specific electron diffraction from a single crystal and the rings are due to the diffraction from multiple crystals. SAED analysis was performed simultaneously in 30c, 200c, 1M and 10M potencies of *Platina* during the experiment (►**Figs. 2C**, **3C**, **4C** and **5C**). Analysis of the d-space value of 30c to 10M potencies of *Platina* confirmed the presence of platinum dioxide (PtO_2).

Control Samples of Alcohol Did Not Show Any Particles

The control samples of alcohol (pharmaceutical grade unsuccussed alcohol and potentised *Alcohol* [6c, 12c and 30c]) were analysed with DLS and HRTEM: no particles were found on either analysis. The DLS analyses of the alcohol con trol samples were blank, without any graph, due to a complete absence of particles in the analysed solution.

HRTEM and EDS Analyses of *Platina* by potency

Weight percentages of the elements present in the NPs were measured using EDS attached to the HRTEM. All the potencies of *Platina* from 30c to CM showed the presence of the element platinum in various weight percentages (►**Table 1**). During the HRTEM analysis, the sizes of NPs were measured. The measurement given shows the size of the smallest and the largest particles in the fields (►**Table 2**).

Platina 30C

Particles were identified in *Platina* 30c (►**Fig. 2A, B**). The size of particles measured was between 3.31 and 12.7 nm. Particles were seen isolated as well as in aggregation. On EDS, the weight percentage of platinum was 16.93 and iron was 83.07 (►**Supplementary file 3.1**, available online only—EDS

Table 1 Comparative statement of the weight percentage of elements in *Platina* 30c–CM.

Potency	Elements					
	Pt	C	Cu	Fe	Zn	Hf
Platina 30c	16.93			83.07		
Platina 200c	2.32	96.51	1.17			
Platina 1M	32.74		39.39		27.86	
Platina 10M	19.62		74.91	5.48		
Platina 50M	0.68	99.32				
Platina CM	44.48					55.52

Table 2 Size of nanoparticles in various potencies of *Platina* 30c–CM

Potency	Particle size
Platina 30c	3.31–12.7 nm
Platina 200c	0.69–3.01 nm
Platina 1M	2.28–7.89 nm
Platina 10M	3.67–5.51 nm
Platina 50M	2.38–5.99 nm
Platina CM	1.94–8.54 nm

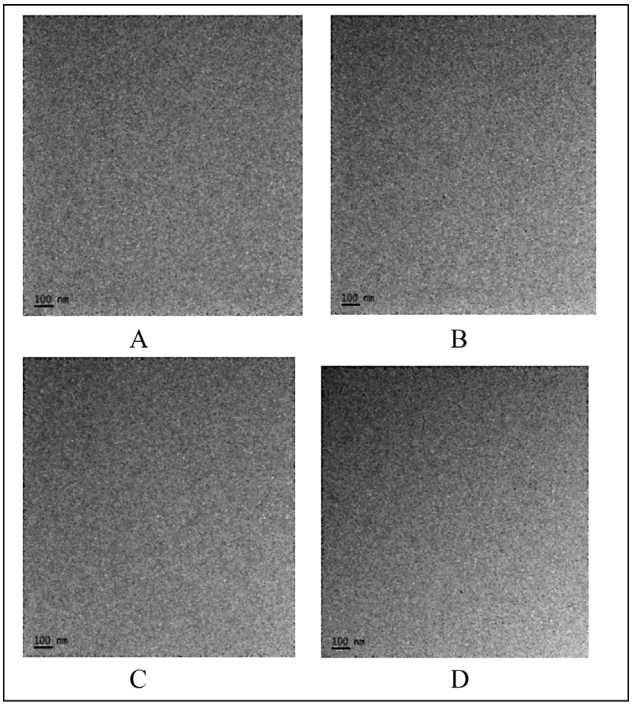

Fig. 8 HRTEM images of pharmaceutical grade unsuccussed alcohol **(A)**, *Alcohol* 6c **(B)**, *Alcohol* 12c **(C)** and *Alcohol* 30c **(D)**; scale bar 100 nm. HRTEM, high resolution transmission electron microscopy.

graph of *Platina* 30c). SAED analysis identified the planes of PtO_2 (►**Fig. 2C**) in *Platina* 30c.

Platina 200C

NPs were detected in different fields (►**Fig. 3A, B**), with particle size 0.69 to 3.01 nm. In 200c *Platina*, EDS analysis revealed the presence of platinum (weight percentage, 2.32), carbon (weight percentage, 96.51) and copper (weight percentage, 1.17) (►**Supplementary file 3.2**, available online only—EDS graph of *Platina* 200c). d-Space analysis using SAED in 200c potency confirmed the presence of platinum in the form of PtO_2 (►**Fig. 3C**)

Platina 1M

In 1M potency *Platina*, particles were identified (►**Fig. 4A, B**) in different fields and the measurement varied from 2.28 to 7.89 nm. EDS analysis of the NPs revealed the weight percentage of platinum as 32.74, copper as 39.39 and zinc as 27.86 (►**Supplementary file 3.3**, available online only—EDS graph of *Platina* 1M). Analysis of the SAED pattern (►**Fig. 4C**) confirmed the presence of PtO_2.

Platina 10M

HRTEM images (►**Fig. 5A, B**) of *Platina* 10M showed unique clusters and a large number of independent particles in different fields. The particle size measured was 3.67 to 5.51 nm. EDS analysis was confirmatory for platinum (weight percentage, 19.62), copper (74.91) and iron (5.48) (►**Supplementary file 3.4**, available online only—EDS graph of *Platina* 10M). d-Space analysis by SAED (►**Fig. 5C**) showed that platinum was present as PtO_2.

Platina 50M

HRTEM images of *Platina* 50M (►**Fig. 6A, B**) showed the presence of NPs in various fields. Particles were seen in isolation as well as in aggregation, with the size ranging between 2.38 and 5.99 nm. EDS showed that weight percentage of platinum was 0.68 and carbon 99.32 (**Supplementary file 3.5** available online only—EDS graph of *Platina* 50M).

Platina CM

In CM potency *Platina*, HRTEM analysis (►**Fig. 7A, B**) showed the presence of particles in various fields. Particles were between 1.94 and 8.54 nm. EDS analysis of the NPs showed the weight percentage of platinum as 44.48 and hafnium as

55.52 (**Supplementary file 3.6** available online only—EDS graph of *Platina* CM).

HRTEM Analyses of Control Samples (Pharmaceutical Grade Unsuccussed Alcohol and Potentised *Alcohol*)

HRTEM images of pharmaceutical grade alcohol (►**Fig. 8A**), *Alcohol* 6c (►**Fig. 8B**), *Alcohol* 12c (►**Fig. 8C**) and *Alcohol* 30c (►**Fig. 8D**) did not show the presence of any particle in the fields.

Discussion

The analysis of *Platina* 30c to CM potencies, and pharmaceutical grade unsuccussed alcohol and potentized *Alcohol* (6c, 12c and 30c), has given some clear results. The observations of alcohol control samples under DLS and HRTEM did not show any particles. DLS analysis of *Platina* showed the presence of NPs in all potencies. The analyses of the samples of *Platina* with HRTEM, EDS and SAED consistently showed the presence of platinum in the drug solutions. The findings prove that *Platina* prepared by homeopathic potentization had generated NPs in all the high dilutions, further strengthening the nanopharmacological paradigm in homeopathy.

The DLS analysis of *Platina* showed the presence of NPs in all sample solutions, with a mean particle size that varied from 1.3 nm in 30c to 6.5 nm in the CM potency. The smallest mean particle size was measured in 1M (0.7 nm) and the largest in CM (6.5 nm). In the HRTEM analysis of *Platina,* there were NPs in all sample potencies. The smallest NPs were measured in 200c (0.69 nm) and the largest in 30c (12.70 nm). The NPs of all other potencies seen were within this range. It is also observed that the NPs formed in the homeopathic manufacturing process are poly-dispersed, not mono-dispersed as in the case of manufactured NPs in nanotechnology.

In DLS, the mean particle size of the NPs in the solution is measured, whilst in the HRTEM a micro-drop of the solution is used for the analysis and only one selected area of the TEM grid is scanned at a time to identify the particles and measure their size. Therefore, there could be variations in the measurement of the particle size in the same samples by DLS and HRTEM.

EDS analysis of *Platina* showed the presence of the element platinum in 30c, 200c, 1M, 10M, 50M and CM potencies. Elements like C, Cu, Fe, Zn and Hf were also found in the fields during the study. Among the extra elements found, C and Cu are part of the TEM grid and the exposure to EDS beams can show their presence. The presence of C may increase further due to its presence in the vehicle (sugar of milk) used for the initial stages of preparation of *Platina*. Presence of Hf is a common machine error in the reading. Therefore, the actual weight percentage of Pt might be much higher than the measured values. The observation of the presence of iron and zinc might indicate impurities that may have originated from the triturated lactose, air contaminants or from containers[17]. EDS analysis is sensitive to beam parameters, topography of sample, acquisition settings, electronic and external field noises, and the atomic number of elements. Therefore the values detected may not be absolute.

SAED analysis of *Platina* identified planes of PtO_2 in the 30c, 200c, 1M and 10M potencies of *Platina*. Platinum is a noble metal and it is not oxidised in nature, but the UHPs of *Platina* showed platinum dioxide in all the analysed samples. It is very interesting to note that platinum is oxidised during the process of homeopathic potentization. A toxic effect of platinum NPs reported[18,19] elsewhere has never been observed in homeopathic clinical practice using UHPs of *Platina*. Oxidised platinum in nanoscale might be the reason for the non-toxic therapeutic action of UHPs of *Platina*. The process of potentization in liquid media (pharmaceutical grade alcohol) is unique in the manufacturing of homeopathic UHPs. The solution is powerfully shaken up in a glass container, which generates a large number of NPs. The kinetic energy released during the process of succussion (potentization) could be the factor helping in the formation of NPs and the oxidation of platinum.

DLS and HRTEM analysis of pharmaceutical grade alcohol and the potentized control samples did not show any particles, whereas the original drug substance was consistently seen in all UHP preparations of *Platina.* These observations are very relevant for future studies on the science of homeopathy.

As the nanoparticulate nature of homeopathic UHPs has been characterised repeatedly[1–10,14] it is relevant to know how it would influence epigenetic programming in the human genetic system: i.e. in drug-proving experiments and in the context of curative or palliative effects. Many publications have probed the biological action[20–33] of homeopathic UHPs. Since NPs of smaller size (<10 nm) have unique chemical, physical and mechanical properties, they can easily penetrate into the cell and nucleus[34] and are able to directly interact with the genetic system:[35] this opens up vast scope for further research within the medical world.

Conclusion

This study confirms the presence of the source material, platinum, in all UHPs of *Platina* and the total absence of particles in the alcohol control samples. It shows that presence of the source material in the primary step of potentization is essential to generate NPs in UHPs. The size of NPs of *Platina* is mostly less than 10 nm, which gives them exceptional capability for size-dependent nuclear entry. The particles are polydispersed, not mono-dispersed as in the case of manufactured NPs. Presence of NPs of the source material in all UHPs would point toward nanopharmacology as the therapeutic basis for homeopathy. The SAED analysis of 30c, 200c, 1M and 10M potencies showed the presence of platinum dioxide. Therefore, it is clear that homeopathic potentization is an effective method to oxidise the noble metal platinum to platinum dioxide, thereby nullifying its toxic effects. Further studies based on these findings may bring more definite answers to the question about the therapeutic properties of UHPs.

Highlights

- HRTEM (high resolution transmission electron microscope) and EDS (energy dispersive spectroscopy)

studies revealed that UHPs of *Platina* contain NPs of the original source material (platinum).
- SAED (selected area electron diffraction) analysis of *Platina* UHPs showed that platinum is present as platinum dioxide.
- Unsuccussed and potentized *Alcohol* samples did not contain any particles.

Supplementary material

Supplementary file 1. DLS analysis of *Platina.*
Supplementary file 2. DLS analysis of pharmaceutical grade unsuccussed alcohol and potentised Alcohol.
Supplementary file 3. EDS graph of *Platina* 30c to CM potencies.

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Conflict of Interest
None declared.

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