

Research Article

Calculation strategies of molar ratio based homeopathic dilutions and the need for pharmaceutical scientists' engagement

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ABSTRACT

Purpose: A deficit was identified in the traditional method of making homeopathic dilutions by 1:9 or 1:99 serial dilutions based on the physical units of mass or volume. When the chemical unit mole is considered, the 1:9 mass-based dilution of nitroglycerin in ethyl alcohol has a 1:48.8 molar ratio. In order to provide the 1:9 molar ratio, the mass ratios required for formulations with lithium carbonate: lactose (diluent) and lead phosphate: lactose are 1:41.7 and 1:3.8 respectively. The extreme incongruity between the mass and the volume-based 1:9 ratios and the ratios based on chemical unit mole show the need to adopt the later scheme which is based on sound principles of chemistry.

Method: Detailed calculations in determining the 1:9 molar ratio of drug: diluent are explained. Method for the molar ratio calculation of chemically less defined medicines such as plant extracts are proposed.

Results: A Molar Ratio Universal Formula for the calculation of the amount of diluent to be used in preparing a given potency of a homeopathic preparation is introduced.

Conclusion: The molar ratio dilutions based on principles of chemistry stand for wider acceptance of homeopathic medicines by the scientific community and for the advancement of the homeopathic system of medicine.

Keywords

Molar ratio potency (mX); Molar Ratio Universal Formula (MRUF); Homeopathic dilution; Opium alkaloids; Weighted average molecular weight

INTRODUCTION

Homeopathy is an essentially European system of medicine as it was conceived, developed and fully established there before

spreading into the rest of the world.(1-2) It is the second most widely prevailing system of medicine in the world, enjoying at present another phase of popularity with a push for



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integration with modern medicine.(3) An entire section of the British Pharmacopoeia is dedicated to Homeopathic medicine and warrants pharmaceutical scientists to have a fresh look at the pharmaceuticals of homeopathic preparations.(4) Since the discovery of homeopathy in 1796 by the German physician Dr. Samuel Hahnemann (April 10th, 1755–July 2nd, 1843) its inventory of medicines now adds up to over 6500.(5) Some of the books carry over 1000 monographs of homeopathic medicines.(6) This monumental development in homeopathic medicines has not been adequately addressed and matched by the contributions of modern-day pharmacists and chemists.

The recent emergence of an intricate photon-based delayed luminescence analytical procedure carried out by a group of German and Indian scientists is very significant. It determines the identity of an unknown medicine as well as the potency in high dilutions of homeopathic formulations free of material drug and should effectively put an end to the claim that nothing exists in high potencies.(7) The discovery claims that regular analysis of non-material high homeopathic potencies may become a reality in due course. Pharmaceutical scientists need to partner with this fascinating new discovery that has given credibility to the mode of action of homeopathic high potencies.

The system of homeopathic medicine is based on a number of cardinal principles (seven principles) unique to it.(8,9) The booklet referred here succinctly explains homeopathy and the universal general medical principles that may broaden our overall outlook towards medicines and therapeutics of all medical systems. All the popular medicinal plants are common to both modern medicine and homeopathy. Where it

differs is the way in which the medicines are prepared and prescribed to the patients.

The homeopathic dilutions are currently prepared without any regard to concentration of the constituent 'formula units' of atoms, molecules or ions of the active ingredient. It is proposed that the unit of reference in the 1: 9 ratio should be the number of molecules or moles of the drug: diluent for homeopathy formulations.

At present in the preparation of decimal scale dilutions represented by the symbol X, the starting raw material and thereafter every preceding dilution is serially diluted in a 1: 9 mass or volume ratio during production of homeopathic formulations. The degree of dilution will increase as 1/10, 1/100, 1/1000, 1/10000 and such wise. In the centesimal scale dilutions, symbol C, are prepared similarly in a 1: 99 dilution ratio. The degree of dilution will increase as 1/100, 1/10000, 1/1000000, 1/100000000 and such wise at each dilution stage.(10-11) Basic principles relevant to molar ratio potencies were described in another article.(12) Symbol assigned for molar ratio potencies are mX for decimal and mC for centesimal series.

The 'nine classes' classification according to the 'old method' in homeopathy is meant to minimize the differences in the strength of mother tinctures prepared from widely differing raw materials.(13) A classification similar to the nine classes of the old method is given in the 'eleven methods' of mother tincture preparation in The British Pharmacopoeia 2012. British Pharmacopoeia 2020 gives the same but in greater detail. The proposed 'Molar ratio scheme' of dilution will eliminate all traces of inconsistencies in dilution processes in both series of dilutions either in ethyl alcohol or lactose.

In the nominal mass or volume-based dilutions, the 1:9 physical ratio is maintained while the ratio of moles or the molecules of the drug: diluent keep changing depending on the drug and the diluent used. Under molar ratio scheme, number of molecules remain fixed at 1:9 independent of the molecular weight of the drug substance or the diluent while the mass or volume ratios of the drug: diluent are subjected to changes.

MATERIALS AND METHODS

The term molar ratio in the decimal series represents that for each mole or molecule of the active drug substance there shall be 9 moles or molecules of the diluent in the molar ratio dilution for the first potency, 1 mX. Similarly, for each mole or molecule of the active drug substance there shall be 99 moles or molecules of the diluent in the molar ratio dilution for the second potency, 2 mX and such wise.

The molar ratio principle is limited to

24 mX and 12 mC dilutions since no molecules could be found in higher potencies according to calculations based on the Avogadro constant.

The masses representing drug: diluent 1:9 molar ratio potencies at dilutions higher than 4 mX- 6 mX potencies converge on nominal mass or volume 1:9 ratio similar to the conventional potencies (Table 1).

Therefore, among thousands of dilution steps the molar ratio scheme is limited only to the first 4 mX– 6 mX potency steps greatly facilitating the adoption of the new scheme.

To explain the differences between the regular potencies and the proposed molar ratio potencies, a model calculation for nitroglycerin (*Glonoine*) in ethyl alcohol for the first potency in the respective decimal scale 1 X and molar ratio 1 mX is given below. Nitroglycerin and ethyl alcohol are taken in weighed amounts for the preparation of potencies.

Table 1. Molar ratio decimal scale mX potency series of nitroglycerin in ethyl alcohol showing relationship between masses and molecules

Molar ratio potency stage (mX)	Mass taken from previous step (g)	Fresh diluent Required to adjust molar ratios (g)	Potency end mass* (g)	Number of moles in nitroglycerin fraction in end mass (Mole)	Number of molecules in nitroglycerin fraction in the end mass
1 mX	1.0 (raw drug)	1.8258	2.8258	4.4035×10^{-3}	2.6518×10^{21}
2 mX	1.0 of 1 mX	6.4612	7.4612	1.5583×10^{-3}	9.3841×10^{20}
3 mX	1.0 of 2 mX	8.6597	9.6597	2.0885×10^{-4}	1.2577×10^{20}
4 mX	1.0 of 3 mX	8.9647	9.9647	2.1621×10^{-5}	2.8151×10^{19}
5 mX	1.0 of 4 mX	8.9964	9.9964	2.1697×10^{-6}	1.3066×10^{18}
6 mX	1.0 of 5 mX	8.9996	9.9996	2.1705×10^{-7}	1.3070×10^{17}
7 mX	1.0 of 6 mX	8.9999	9.9999	2.1706×10^{-8}	1.3071×10^{16}
8 mX	1.0 of 7 mX	8.9999	9.9999	2.1706×10^{-9}	1.3071×10^{15}
9 mX	1.0 of 8 mX	8.9999	9.9999	2.1706×10^{-10}	1.3071×10^{14}
-----	-----	-----	-----	-----	-----
21 mX	1.0 of 20 mX	9	10	2.1706×10^{-22}	130
22 mX	1.0 of 21 mX	9	10	2.1706×10^{-23}	13
23 mX	1.0 of 22 mX	9	10	2.1706×10^{-24}	1.3

*End mass = {Mass of 1 g from previous potency step (includes the portion of drug in diluent)} + (Mass in g of fresh ethyl alcohol required to adjust the molar ratio of the respective dilution step); mX: Decimal scale molar ratio potencies; g: Gram.

Determination of the molar (molecular) ratio of the conventional mass ratio 1:9 nitroglycerin:ethyl alcohol: The calculations indicated below are only for the ethyl alcohol based liquid potencies. Similar set of calculations are required for solid anhydrous lactose-based potencies of the medicines prepared by trituration. Molecular weight of ethyl alcohol must be substituted with lactose anhydrous (molecular weight: 342.3 g.mol⁻¹) as appropriate.

The regular decimal scale mass based 1:9 dilution ratio consists of 1 part by mass of nitroglycerin (molecular weight: 227.09 g.mol⁻¹) in 9 parts by mass of ethyl alcohol (molecular weight: 46.07 g.mol⁻¹) for the 1X potency. There is no other consideration in assigning the ratio 1:9 here.

The number of moles of nitroglycerin =
 $1 \text{ g} / 227.09 \text{ g.mol}^{-1} = 0.0044 \text{ mol}$

Similarly,

The number of moles of ethyl alcohol =
 $9 \text{ g} / 46.07 \text{ g.mol}^{-1} = 0.1954 \text{ mol}$

Therefore,
 nitroglycerin: ethyl alcohol molar ratio =
 0.0044:0.1954,
 or
 1:(0.1954/0.0044)
 or 1:44.4091

The conventional 1:9 nominal mass ratio represents a 1:44.4091 molar ratio for the first decimal potency *Glonoine* 1X. This means for each single nitroglycerin molecule there are 44.3988 ethyl alcohol molecules, far in excess of the expected 1:9 molecular ratio under the proposed scheme. This is almost five times more dilute than it appears nominally ($44.4091/9 = 4.9343$). In stoichiometric terms it amounts to an excess of diluent molecules of nearly 500%.

Determination of mass ratio of nitroglycerin:ethyl alcohol under the proposed 1:9 molar ratio for 1mX potency: Calculations to determine the masses required for 1:9 molar ratio-based dilution for the first potency of *Glonoine* 1mX in ethyl alcohol is described here. The actual masses to be used in the preparation of the first decimal molar ratio potency can be found out by multiplying 1 molecule of nitroglycerin and 9 molecules of ethyl alcohol by their respective molecular weights.

Mass of nitroglycerin required for the first decimal molar ratio potency; 1mX
 $= 1 \text{ mol} \times 227.09 \text{ g.mol}^{-1} = 227.09 \text{ g}$

Mass of ethyl alcohol required for the first decimal molar ratio potency; 1mX
 $= 9 \text{ mol} \times 46.07 \text{ g.mol}^{-1} = 414.63 \text{ g}$

The ratio of masses of nitroglycerin to the diluent = 227.09 g:414.63 g,
 or 1 g:(414.63/227.09) g,
 or 1:1.8258

For these two substances, 1:9 molar ratio dilution is represented by a mass ratio of 1:1.8258 parts of nitroglycerin: ethyl alcohol for the first decimal molar ratio potency 1mX. The calculations up to this point convincingly display the inconsistencies in the strength at molecular level in the nominal mass ratio-based dilutions.

Calculations for the 2 mX, 3 mX and higher dilution steps are somewhat complex. The solvent molecules from the previous dilution gets dragged into the next higher dilution along with the required number of active ingredient molecules. An adjustment for these excess diluent molecules has to be made at each dilution step by deducting these from the calculated amount of diluent to

arrive at the correct molar ratio because this is a serial dilution process.

Determination of masses required for molar ratio dilution of the drug *Glonoine*

2 mX potency: The stepwise calculation of the second decimal scale molar ratio potency *Glonoine* 2mX which has a molar ratio of 1:99 of *Glonoine*:ethyl alcohol is as follows. From the second dilution step onwards, the amount of diluent present in the 1.0 g of the previous potency must be deducted from the calculated value of the diluent in order to maintain the required drug:diluent molar ratio. This applies for the preparation of all homeopathic molar ratio potencies 2 mX upwards.

1. Take 1.0 g from the previous dilution *Glonoine* 1mX.

2. Mass of active ingredient in the 1.0 g sample of *Glonoine* 1mX

= Mass (g) of the previous dilution taken \times $\frac{\text{molecular weight of } Glonoine}{[\text{molecular weight of } Glonoine + (\text{proportion of ethyl alcohol moles in previous dilution} \times \text{molecular weight of ethyl alcohol})]}$

$$= \frac{1.0 \text{ g} \times 227.09 \text{ g} \cdot \text{mol}^{-1}}{227.09 \text{ g} \cdot \text{mol}^{-1} + (9 \text{ mol} \times 46.07 \text{ g} \cdot \text{mol}^{-1})}$$

$$= 0.3538 \text{ g}$$

$$= 0.3538 \text{ g}$$

3. Number of moles of *Glonoine* in 0.3538 g
 $= 0.3538 \text{ g} / 227.09 \text{ g} \cdot \text{mol}^{-1} = 0.00156 \text{ mol}$

4. Number of moles of solvent ethyl alcohol needed to achieve 1:99 molar ratio of the 2 mX potency

$$= 0.00156 \text{ mol} \times 99 = 0.15426 \text{ mol}$$

5. The mass of 0.15426 mol of ethyl alcohol
 $= 0.15426 \text{ mol} \times 46.07 \text{ g} \cdot \text{mol}^{-1} = 7.1067 \text{ g}$

6. Therefore, the total mass of solvent needed for the second decimal molar ratio potency = 7.1067 g

7. According to step 2 above, the amount of solvent ethyl alcohol in 1.0 g sample of the previous dilution 1mX

$$= 1.0 \text{ g} - 0.3538 \text{ g} = 0.6462 \text{ g}$$

8. Therefore, the mass of the fresh amount of solvent to be added

$$= 7.1067 \text{ g} - 0.6462 \text{ g} = 6.4605 \text{ g}$$

9. To prepare the second decimal molar ratio potency, take 1.0 g of *Glonoine* 1mX potency, add and mix 6.4605 g of ethyl alcohol and apply ten strokes to yield 7.4606 g (1g + 6.4606 g) of *Glonoine* 2mX potency.

Multiples of the amounts of *Glonoine* 1mX potency and ethyl alcohol by the same factor may be used for the purpose. E.g. 10{(1.0) : (6.4606)} *Glonoine* 1 mX : ethyl alcohol.

Determination of masses required for molar ratio potency of the drug *Glonoine*

3mX and higher: Carry out calculation steps 1 to 9 on the same basis as for *Glonoine* 2 mX under the section immediately before this.

Under the above step 2 calculation of the 2mX potency, 9 should be substituted with 99 in the denominator of the mathematical fraction. This is because 1:99 is the molar ratio dilution in the 1 g quantity of the 2mX potency used. Proceed with calculations similar to the 2mX potency above but using 1:999 as the molar ratio in the step 4. The calculation should be repeated for higher dilution steps replacing 9 in the mathematical fraction in the step 2, with the molar ratio number of the diluent of the previous potency and molar ratio of the potency stage being processed in the step 4.

Differences in the molar ratios of the drug: diluent at different potency stages resulting under the conventional 'mass based' and 'molar ratio' based dilutions of

nitroglycerin in ethyl alcohol were compared using bar charts (Figure 1). The value for the first potency stage of the 1:9 conventional mass-based dilution ($1/44.3988 = 0.0225$) is equivalent to molar ratio $1/9 = 0.1111$.

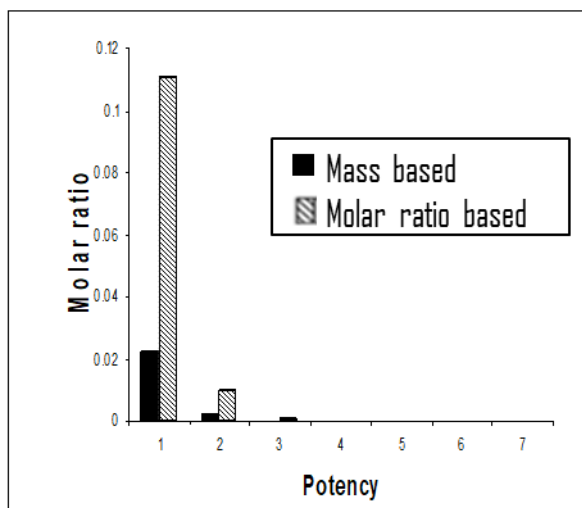


Figure 1: Comparison of decimal scale molar ratios (drug/diluent) in dilution stages of *Glonoine* in ethyl alcohol in the regular mass-based potencies and molar ratio based potencies

Molar Ratio Universal Formula (MRUF) and Reduced Molar Ratio Universal Formula (RMRUF) for the determination of the mass of the diluent required for the potency development: A MRUF was constructed by the authors to facilitate calculations in the preparation of advancing molar ratio potencies. It was derived based on the calculation steps 1 to 8 above for the determination of the amount of solvent required for the 2 mX potency. It determines the mass of diluent, ethyl alcohol or lactose anhydrous to be incorporated in the preparation of the next higher potency. The formula accommodates variations due to ever changing molecular weights of the raw medicines and also the diluent employed. The use of the formula is convenient as the values to be substituted in the formula are readily available.

Alternatively, the simplified RMRUF shown below the MRUF can also be used for the calculation purpose.

Proposed MRUF for the determination of the required amount of fresh diluent for the next higher potency, for a given amount of a drug or dilution =

$$\left[\left\{ \frac{A \times B}{B + (C \times D)} \right\} / B \right] \times (E \times D) - \left[A - \left\{ \frac{A \times B}{B + (C \times D)} \right\} \right]$$

Proposed RMRUF for the determination of the required amount of fresh diluent for the next higher potency, for a given amount of a drug or dilution =

$$(n/B) \times (E \times D) - (A - n)$$

It must be noted that in preparing 1 mX potency, the formula yields the mass of the raw drug.

Where,

A: Mass of the dilution/raw drug taken from the previous step (g)

B: Molecular weight of the active ingredient ($\text{g} \cdot \text{mol}^{-1}$)

C: Molar ratio proportion of the diluent of the previous potency. In preparing 1 mX potency this value is 0 since raw drug is free of diluent.

D: Molecular weight of the diluent ($\text{g} \cdot \text{mol}^{-1}$)

E: Molar ratio proportion of the diluent required for the next higher dilution

$$n: \left\{ \frac{A \times B}{B + (C \times D)} \right\}$$

Relationship of masses and number of molecules in 1:9 molar ratio potencies:

With the advancing molar ratio potencies, the calculations demonstrated how every trace of molecules cease to exist beyond 24 mX (or 12 mC) potencies according to the

Avogadro constant (Table 1). The amounts of active ingredient present in material form in 1 part of the previous potency and the amount of diluent required for the potency being prepared for various medicines can be determined by using a similar set of calculations as discussed above. These quantities are illustrated for four medicines, lithium carbonate (molecular weight: 73.89 g.mol⁻¹) in lactose anhydrous (molecular weight: 342.3 g.mol⁻¹), formic acid (molecular weight: 46.02 g.mol⁻¹) in ethyl alcohol (molecular weight: 46.07 g.mol⁻¹), lead phosphate (molecular weight: 811.59 g.mol⁻¹) in lactose anhydrous and nitroglycerin (molecular weight: 227.09 g.mol⁻¹) in ethyl alcohol (Table 2). Based on the molecular weights of the drug and the diluent involved, the four medicines are listed in the ascending order of the amounts of the material drug present in 1 part of the previous potency. Due to similarities in their molecular weights, formic acid in ethyl alcohol requires a nearly constant mass ratio of 1:9 for all potency steps. Table 2 shows that around the 4mX potency, the other three medicines converge on 1:9 mass ratios similar to the regular decimal potencies.

Molar ratio potencies of medicines consisting of mixtures of chemicals: The following three approaches can be suggested for the medicines consisting of mixtures of chemicals in plant and animal extracts.

- i. Scheme 1: It can be based on the principle of 'marker' substance (14) of herbal medicines. The molecular weight of the marker can be used for the calculations in assigning molar ratios. Opium dried powder contains on the average the following mixture of alkaloids; morphine 12%, codeine 1.6%, thebaine 1.3%, papaverine 1.5%, noscapine 6% and narceine 1% in weight by weight percentages.(15) Morphine can be considered as the marker for opium. Calculation should be adjusted so that for

each molecule of morphine there should be 9 molecules of diluent for the 1mX potency and such wise.

- ii. Scheme 2: It is based on the 'weighted average molecular weight' of a selected group of pharmacologically similar substances. The selected ingredients which are known to be positively active and are having a close range of molecular weights are best considered for the calculation. This appears to be better suited for the purpose than the 'marker' substance when the molecular weight of the 'marker' is not a representative of the group of substances.
- iii. Scheme 3: The weighted average molecular weight of all of the chemically characterized active substances in the mixture can also be considered.

None of these may be practically useful if the calculated amount of diluent does not exceed the amount of the mixture containing the active materials drawn for the dilution making process. This is on account of the fact that there is a large amount of material unrelated to molar ratio scheme is drawn in, over 75% in the case of opium.

Calculation of the weighted average molecular weight of opium alkaloids: The individual molecular weights and the percentages of each alkaloid in the mixture are integrated and represented in the weighted average molecular weight. The result 293.71 g.mol⁻¹ for the four selected opium alkaloids is given in Table 3. For the molar ratio potencies 293.71 g.mol⁻¹ must be used. The alkaloids noscapine and narceine are not considered since their molecular weights are substantially different to the other alkaloids.

The weighted average implies that instead of the mixture of alkaloids there is a virtual single alkaloid with a molecular weight of 293.71 g.mol⁻¹ present at a concentration of 16.4 % in dried opium.

Table 2. Calculated values of material drug present in 1 part of the previous potency and fresh diluent required to adjust molar ratio decimal scale mX potencies

Molar ratio potency stage	Required drug :diluent molar ratio (Mole)	Mass taken from previous potency[Amount of material drug in the mass taken is shown in parenthesis] (g)	Mass of fresh diluent needed to yield there required molar ratio (g)
1mX	1:9	1 of raw drug [1 <i>Lithium carb.</i>] 1 of raw drug [1 <i>Formic acid</i>] 1 of raw drug [1 <i>Plumb phos.</i>] 1 of raw drug [1 <i>Glonoine</i>]	41.6930 Lactose 9.0098EtOH 3.7958 Lactose 1.8258 EtOH
2mX	1:99	1 of 1 mX[0.0234 <i>Lith carb.</i>] 1 of 1 mX[0.0999 <i>Formic acid</i>] 1 of 1 mX[0.2085 <i>Plumb phos.</i>] 1 of 1 mX [0.3539 <i>Glonoine</i>]	9.7657 Lactose 9.0009 EtOH 7.9149 Lactose 6.4612 EtOH
3mX	1:999	1 of 2mX[0.0022 <i>Lith carb.</i>] 1 of 2 mX[0.0099 <i>Formic acid</i>] 1 of 2 mX[0.0234 <i>Plumb phos.</i>] 1 of 2 mX[0.0474 <i>Glonoine</i>]	9.0711 Lactose 9.0000 EtOH 8.8783 Lactose 8.6597 EtOH
4mX	1:9999	1 of 3 mX[0.0002 <i>Lith carb.</i>] 1 of 3 mX[0.0009 <i>Formic acid</i>] 1 of 3 mX[0.0024 <i>Plumb phos.</i>] 1 of 3 mX[0.0049 <i>Glonoine</i>]	9.0071 Lactose 9.0000 EtOH 8.9877 Lactose 8.9648 EtOH
5mX	1:99999	1 of 4 mX[-- <i>Lith carb.</i>] 1 of 4 mX [-- <i>Formic acid</i>] 1 of 4 mX[-- <i>Plumb phos.</i>] 1 of 4 mX[0.0005 <i>Glonoine</i>]	9.0007 Lactose 9.0000 EtOH 8.9988 Lactose 8.9965 EtOH
6mX	1:999999	1 of 5 mX [-- <i>Lith carb.</i>] 1 of 5 mX[-- <i>Formic acid</i>] 1 of 5 mX[-- <i>Plumb phos.</i>] 1 of 5 mX[-- <i>Glonoine</i>]	9.0000 Lactose 9.0000 EtOH 9.0000 Lactose 9.0000 EtOH

mX: Decimal scale molar ratio potencies; g: Gram, carb: carbonicum, phos: phosphoricum, EtOH: Ethyl alcohol

Table 3. Calculation of the weighted average molecular weight of opium alkaloids

(a) Alkaloid	(b) Percentage w/w alkaloids in dried opium	(c) Molecular weight of the alkaloids (g.mol ⁻¹)	(d) Contribution to weighted average molecular weight (b)x(c) (g.mol ⁻¹)
Morphine	12.0%	285.34	3424.08
Codeine	1.6%	299.36	478.98
Thebaine	1.3%	311.37	404.78
Papaverine	1.5%	339.39	509.08
Noscapine	6.0%	413.42	---
Narceine	1.0%	443 46	---
Total contribution of the four alkaloids =			4816.92
Total of the percentage contribution of the four alkaloids (12+1.6+1.3+1.5) =			16.4
Therefore, the weighted average molecular weight =			4816.92/16.4= 293.71

The ‘simple numerical average molecular weight’ of all the alkaloids is not appropriate because the contribution by the varying percentages are not represented. The numerical average molecular weight of the four alkaloids would be $(285.34 + 299.36 + 311.37 + 339.39) \text{ g.mol}^{-1}/4 = 1235.46 \text{ g.mol}^{-1}/4 = 308.86 \text{ g.mol}^{-1}$. This is closer to thebaine 1.3 % which is not as active as morphine. Another alternative is to employ isolated pure alkaloid mixtures from plant materials for similar calculations for molar ratio potency development.

Because of the low concentration of drug substances in extracts, to facilitate the production of molar ratio potencies it may be necessary to prepare ‘mother tincture concentrates’ by suitable processes such as vacuum evaporation. The traditional symbol for mother tinctures 'ø' can be revised as '[ø]' where square brackets symbolize concentration as in chemistry. It is possible to concentrate mother tinctures in to thick pasty masses which in turn may be converted to dry powders similar to Standardized Belladonna Leaf Dry Extract of the British Pharmacopoeia 2012.(16) For low strength mother tinctures or concentrates, for the initial step 2 mX decimal scale potency of 1:99 ratio may have to be prepared instead of 1 mX. The schemes presented here provide a reasonable basis for molar ratio calculations for mixtures of substances that would cover a large number of plant extracts. Where ‘volume’ measures are used for liquid medicines and ethyl alcohol, they must be converted into mass before subjecting them to molar ratio calculations.

RESULTS

Disparities between the molecular ratios at a given dilution step of the medicinal substance and the diluent in the conventional mass based and molar ratio-based potencies are shown in Figure 1 for nitroglycerin in ethyl alcohol. It is at a maximum at the first

potency 1mX. Since the development of higher potencies are based on the first potency, it is most important that all preparations are made uniform in their molar ratios starting from the first potency.

According to Table 1, it is clear that for all practical purposes, molar ratio would be applicable up to 4 mX – 6 mX potencies. The fourth column of Table 2 shows the widely varying masses (or parts) of the two diluents lactose anhydrous and ethyl alcohol required for four medicines representing the decimal scale molar ratios of the particular dilution step. These differences are most obvious in the first potency 1 mX. It shows that the nominal mass or volume-based dilution procedure currently being used is in complete disarray with the fundamentals of chemistry. The amount of material drug found in the aliquot drawn from the previous potency is shown in parenthesis in the third column of Table 2. These were determined by using the calculation schemes given in the previous three sections on “calculating molar ratio dilutions of the drug *Glonoine* 1 mX, 2 mX and 3 mX potencies”.

It must be noted that under molar ratio scheme at each dilution step 1 g of the previous potency is taken for the potency development process. This scheme facilitates the manufacturing process in which only the diluent masses keep changing. The diluent masses required under molar ratio potencies are in sharp contrast to the 1:9 mass ratios in the conventional decimal scale potencies. The very first set of calculations on conventional potencies above shows that since molar ratio of 1:44.39 nitroglycerin:ethyl alcohol was found instead of the expected 1:9 molar ratio, there are an equivalent of $44.39 - 9 = 35.39$ unaccounted stray diluent molecules falling outside the molar ratio scheme. These excessive molecules may not be subjected to the expected effects of stroking or rubbing

during the potentization process. Under conventional potencies the number of stray molecules keep changing chaotically from drug to drug.

Calculations in the Table 2 show the minimum variation to the 1:9 masses when the molecular weights of the drug substance and the diluent are very similar as in the case of formic acid (molecular weight: 46.02 g.mol⁻¹) and ethyl alcohol (molecular weight: 46.07g.mol⁻¹).

DISCUSSION

The molar ratio concept has brought to light another deficiency in the homeopathic preparation of solid medicines even in the conventional centesimal and decimal scale potencies. This is about getting an effective molecular distribution of the solid drug substance in the solid diluent lactose.(17) In the liquid potencies, uniform molecular distribution is assumed to be spontaneous. It is obvious that in the conventional potencies the differences in the molecular weights of ethyl alcohol (46.07g mol⁻¹) and lactose (342.3g mol⁻¹) invariably lead to differences in the degrees of dilution at molecular level in a given potency. This means liquid and solid potencies are unequal in molecular ratios.

The opinion of the scientific community, the pharmaceutical industry and a section of the medical practitioners is that since potencies higher than 24 mX or 12 mC (Table 1) do not carry any drug molecule, there cannot be any action by these potencies. Such conclusions are arrived with clinical studies by practitioners of regular medicine conducted on a mistaken basis without any regard for the principles unique to homeopathy. Such studies are therefore unscientific in the very design.

With the latest discovery on high potency analysis based on delayed luminescence, it is now understood that photons bound to the diluent ethanol or lactose are responsible for their therapeutic action.(7) Pharmaceutical scientists must partner with this fascinating new discovery that has given credibility to the mode of action of high potencies in the absence of material drug. Molar ratio potencies could strengthen the uniformity of the outcome of these sophisticated analyses.

Homeopathy does not respond when prescribed in the manner of modern pharmaceuticals as practiced in Allopathy. Failure of homeopathy is directly proportional to this increasing trend. Unique manner of case taking, patient individualization, use of repertory (listing all the medicines for a given sign or symptom) for the selection of the drug that is most similar in signs and symptoms to the case in question include some of these principles.

The healthcare professionals who rely on material medicines should have no reason to reject effectiveness of potencies below 12C or 24X. Table 1 indicates the number of molecules present in their billions in a given mass of the potency varying from 6.022×10^{23} to just 2 molecules as the dilutions advance up to 24 mX potency. It must be stated that low material potencies 1X, 3X, 6X, 12X, 1C and 6C are quite popular among the homeopaths. According to Table 1 it is evident that even up to 12 mX molar ratio potency, the preparations contain several billion molecules of the drug in a given amount.

Two research papers on a new series of 'homeopathic summation potencies' were published designed for greater appeal of the medical and scientific communities where the strength of the drug is displayed in the label similar to the modern medicines.(18-19) The inclusion of an entire section on

‘Materials for Use in the Manufacture of Homoeopathic Preparations’ in the British Pharmacopoeia is an indication of the recognition of the scientific and therapeutic merit of homoeopathy.(4) Similarly, the reference to homoeopathic medicines in the official web site of the United States Food and Drug Authority is equally significant in this regard.(20)

This article intends to bring to the attention of the scientists, homoeopathic professionals, particularly the manufacturers, a striking inconsistency in the present manner of processing homoeopathic dilutions. The proposed molar ratio potencies as well as the summation potencies(18-19) are intended to improve the scientific merit of homoeopathic medicines from various angles. A design for an air free fluid jet potentizer was published in order to prepare potencies in a completely air free set up.(21) This will eliminate any air admixture and the effects of oxygen and other reactive gases on the drug during the potentization process.

Calculations for molar ratio potencies have to be performed only once for a given drug and diluent. The molar ratio calculations yield a fixed drug:diluent mass ratio for any given potency step as in Table 2.

CONCLUSION

The study presents the basic principles in establishing molar ratio potencies for homeopathic preparations. Since sources of homeopathic medicines include a large number of plants, animals and minerals each individual drug will have certain adjustments when applying the proposed molar ratio principle.

The time has come for both homeopaths and the scientists to have a fresh look at homeopathic medicines in order to effect improvement to this system of medicine in line with modern scientific principles. An

immense amount of therapeutic potential is held in over 6000 homeopathic medicines.

By reassuring the merit of lower range of potencies (1X – 12X) or the proposed (1 mX – 12 mX) with a label declaring the strength of the preparation that runs in to billions of molecules, it is possible to attract a wider circle of medical practitioners to prescribe homeopathic medicines (Table 1).(19) With the introduction of photon based delayed luminescence analytical procedure, the argument that homeopathic preparations have no material drug will not hold good any longer.(7) Incidentally to the credit of this system, the entire range of homeopathic medicines belong to over-the-counter category with few exceptions.

The only new requirement to implement manufacture of homeopathic molar ratio potencies is a set of calculations on the same basis as described under the sections on “Calculating molar ratio dilutions of the drug *Glonoine* 1 mX, 2 mX and 3 mX potencies”. The introduction of MRUF under this study has greatly facilitated the calculations. There is an urgent need for the adoption of proposed molar ratio potencies in order to regularize potency making process in compliance with modern principles of chemistry. It will also provide a scientific basis for more intricate studies including those related to the high potencies. It must be noted that conversion of solid triturates at 6 mX potency into liquid potencies is outside the scope of molar ratio potencies.

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REFERENCES:

- Lockie A, Geddes N. Complete Guide to Homeopathy: The Principles and Practice of Treatment. 1st ed. DK Publishing; 1995. p.10–17
- Lange A, Gaylord SA. Textbook of Natural Medicine. 5th ed. Vol. 5, Focus on Alternative and Complementary Therapies. Churchill Livingstone; 2020. 25–47 p.
- The European Committee for Homeopathy [Internet]. [cited 2021 Apr 17]. Available from: <https://homeopathyeurope.org/>
- British Pharmacopoeia Commission Office. The British Pharmacopoeia 2012. Vol. IV. London: The stationary office; 2012. 3771 p.
- Remedia homeopathy [Internet]. [cited 2021 Apr 17]. Available from: <https://www.remEDIA-homeopathy.com/shop/>
- Murphy R. Homeopathic Remedy Guide. 2nd ed. New Delhi: Indian Books and Periodicals Publishers; 2000. p. 1919- 1948.
- Lenger K, Bajpai RP, Spielmann M. Identification of Unknown Homeopathic Remedies by Delayed Luminescence. Cell Biochem Biophys. 2013;68(2):321–34.
- Singh M. Questions and answers on Organon of Medicine. Calcutta: Bharat Printing Press; 1967. 2 p.
- Maharashtra Council of Homeopathy - Cardinal Principals [Internet]. [cited 2021 Apr 17]. Available from: <https://www.mchmumbai.org/Details.aspx?ID=8>
- Homoeopathic Pharmacopoeia of India. Vol. I. 1st ed. Delhi: Government of India, Ministry of Health; 1970. p. 17-20.
- Guidelines for Manufacturing Homeopathic Medicines - The Homeopathic Pharmacopoeia of the United States - Preprint [Internet]. [cited 2017 July 15]. Available from: www.hpus.com/Draft-Guidelines-for-Manufacturing-Homeopathic-Medicines.pdf
- Pathirana W, Dissanayake PD. Molar Ratio Rectified Potencies. Homeopathic Links. 2013;26(4/13):252-5.
- Government of India, Ministry of Health and Family Welfare. Homoeopathic Pharmacopoeia of India. Vol. I. 1st ed. Delhi: Government of India, Ministry of Health; 1970. p. 247-253.
- World Health Organization. Quality Assurance of Pharmaceuticals: A Compendium of Guidelines and Related Matters, Good Manufacturing Practices and Inspection. Vol. 2. Geneva: World Health Organization; 2007. 257 p.
- Paul MD. Medicinal Natural Products a Biosynthetic Approach. 2nd ed. West Sussex England: John Wiley and Sons Ltd; 2004. 359 p.
- British Pharmacopoeia Commission Office. The British Pharmacopoeia 2012. Vol. IV. London: The Stationery Office; 2012. 3491p.
- Winfield AJ. Powders and Granules. In: Winfield AJ, Rees JA and Smith I (eds.). Pharmaceutical Practice, 4th ed. Philadelphia: Churchill Livingstone; 2010. 388 p.
- Pathirana W. Introduction to Summation Potencies - Incorporating a Material Dimension to Potencies Past Avogadro's Constant. Homeopathic Links. 2002;15(1/02):40-4.
- Pathirana W. Further studies on summation (s) potencies - Quantitative parameters and clinical efficacy. Homeopathic Links. 2003; 16(3/03):177-180.
- U.S Food and Drugs Administration.

- Homeopathic products [Internet]. 2021 [cited 2021 Dec 11]. Available from: <https://www.fda.gov/drugs/information-drug-class/homeopathic-products>
21. Pathirana W. Blueprint for Designing an Air-Free Fluid Jet Potentizer. *Homoeopathic Links*. 2014; 27(4/14):245-251.