The major objection to homeopathic medicine is that the doses of medicine prescribed in some cases are too dilute for any active ingredient to be present. The medicines would hence be rendered inactive, necessitating novel explanations for the action. A further examination of dilution in the light of the Langmuir equation shows that homeopathic medicines may not be as dilute as a simplistic application of Avogadro’s Principle suggests, due to surface effects. Homeopathy (2014) 103, 143–146.

Keywords: Homeopathy; Ultramolecular dilution; Langmuir equation; Surface effects

Introduction

Homeopathic medicines are in use in large parts of the world and evidence for their effects is well proven in-vitro. The major criticism to homeopathic medicine is that it employs dilutions like 60X (60D or 30C) where the concentration of the active ingredient is $10^{-60}$ times the original concentration. If one assumes the presence of 1 M of the active ingredient in the mother tincture then the probability that one molecule of the active ingredient will be present in a liter of 30C solution would be $6 \times 10^{-37}$, which is fantastically dilute. Arnica 30C, the alcoholic extract of Arnica Montana (containing helenalin amongst other compounds as an active ingredient) diluted $10^{60}$ times is used for its anti-inflammatory and anti-tumor properties. Assuming that mother tincture contained 262.3 g of helenalin in a liter of alcohol, the probability to find one molecule of helenalin in 1 ml of Arnica 30C would be $6 \times 10^{-40}$.

Various attempts have been made to reconcile the action of the drugs at such super-Avogadro dilutions. Recently however, experimental evidences show that more than the expected amount of active materials are present at extreme dilutions in solutions.

Here, a minimal mathematical model of dilutions has been presented, where the role of interfaces on dilution has been taken into account. Avogadro’s law is not questioned, simply the role of surfaces on dilution is stressed. The Langmuir adsorption model is invoked, where a monolayer of molecules is adsorbed in dynamical equilibrium with those in solution. The equilibrium between the adsorbed state and the dissolved state results in an initial linear rise in the adsorbed number with the concentration of the dissolved molecule, later reaching a saturation. The model is not specific to the type of the molecule of the active ingredient or the solvent. The goal of this model is to help reconcile some recent observations of unexpected higher concentrations at high dilutions.

Dilutions

When a solution is recursively diluted, it involves the mixing of $v$ liter of the solution with concentration $c_{n-1}$ moles/liter and mixing $V$ liter of the solvent to give about $v + V$ liter of the solution with a concentration $c_n$. This process assumes the additivity of volumes, which is strictly valid for ideal solutions, is roughly valid for small concentrations $c_{n-1}$ of solute.

The molecules of the active ingredient would not only be dispersed through the bulk of the solvent (both homogeneously and/or by nanostructures) but would also be present on the free surface (solvent—vapor interface) and the solvent—solid interface. Molecules of the active ingredient are physisorbed onto the surface in equilibrium. The iterative-dilution could proceed in the following two ways: (a) the mixing container is not reused (Hahnemannian method of dilution), where a $v$ amount of solution is poured into $V$ volume of solvent, successsed and from it a volume $v$ is poured into the next container of $V$ volume of solvent and this process is repeated, or (b) the mixing container is reused (Korsakovian method of dilution), and in it $V$ amount of solvent is added to an initial volume $v$ of the solution, successsed and the a volume $V$ is poured off, and this process is
repeated. Equilibrium is assumed at all stages. The two processes are treated in the following two subsections.

(a) Situation where the mixing container is not reused (Hahnemannian method of dilution)

In this process, where the glassware is changed at each dilutional step, assuming that the surface density of the active ingredient for the solvent—solid interface is \( \sigma_s \) and that on the free surface it is \( \tau_s \), we have,

\[
c_n(v + V) + \tau_s a' + \sigma_s(a + A) = c_{n-1}v + \tau_{n-1}(a' + a^n).
\]

(1)

where, \( a \) is the original liquid—solid interface area, \( A \) is the liquid—solid interface area after the solvent is added, \( a' \) is the solution-vapor surface area when at rest and \( a'' \) is the increase in the solution-vapor surface area when being poured.

Ignoring \( \sigma \) and \( \tau \) one gets the usual exponential decay of concentration as

\[
c_n = c_0 f^n \quad (2)
\]

which for \( f = 0.1 \) gives \( c_n = c_0 10^{-n} \) as expected.

One simple model for \( \sigma \) and \( \tau \) would be to assume that the molecules on the surface are in dynamic equilibrium with those in the bulk of the solvent. When the solute molecules adsorbed on the surface are in dynamic equilibrium with those in solution, the adsorbed number density (\( \sigma \)) of solute molecules and the dissolved concentration (\( c \)) are related by the Langmuir adsorption isotherm

\[
\sigma = \frac{\sigma_{\text{max}} bc}{1 + bc}
\]

(3)

which is dependent on the temperature \( T \). At very low concentrations (which is true for the dilutions discussed here) the Langmuir equation can be reduced to \( \sigma = \sigma_{\text{max}} bc / (1 + bc) \approx K_c \), where \( b \) is a function of temperature. The equilibrium constants can hence be written as

\[
\frac{\sigma_k}{c_s} = K(T)
\]

(4)

and

\[
\frac{\tau_s}{c_s} = Q(T)
\]

(5)

where \( K \) and \( Q \) are equilibrium constants, which are functions of temperature. Eq. (1) can hence be rewritten as

\[
c_n + Qc_{n-1} + Kc_s(\alpha + \beta) = c_{n-1}f + Qc_{n-1}^l.
\]

(6)

where

\[
\alpha = \frac{a}{v + V}, \quad \beta = \frac{A}{v + V}, \quad \lambda = \frac{a'}{v + V}, \quad \lambda' = \frac{a' + a''}{v + V}, \quad f = \frac{v}{v + V} < 1.
\]

This enables one to write

\[
c_n = c_{n-1} \left( \frac{f + Q\lambda'}{1 + Q\lambda + K(\alpha + \beta)} \right) = c_{n-1} \mu^n
\]

(7)

which gives

\[
c_n = c_0 \mu^n.
\]

(8)

If \( f < Q\lambda/(Q\lambda + K(\alpha + \beta)) \) then \( \mu > f \) and the dilution is slower than perceived. If one uses \( v = 1 \) cm\(^3\), \( V = 9 \) cm\(^3\), \( a = 50.8 \) cm\(^2\), \( A = 4.5 \) cm\(^2\), \( K = Q = 0.07 \) (value of \( Q \) calculated from the data by Chang et al.\(^{15} \) for sodium dodecyl sulfate (SDS) in 0.5 M NaCl solution; it is assumed that \( K = Q, a' = 50.3 \) cm\(^2\), \( a'' = 0.02 \) cm\(^2\), \( a = 5.1 \) cm\(^{-1}\), \( \beta = 0.45 \) cm\(^{-1}\), \( \lambda = 5.027 \) cm\(^{-1}\), \( \lambda' = 5.028 \) cm\(^{-1}\) one gets \( \mu = 0.26 \). This would imply that a 30C dilution is effectively a 17C dilution.

(b) Situation where the mixing container is reused (Kor-sakovian method of dilution)

In this process, where a single piece of glassware is used throughout the process of dilution, assuming that the surface density of the active ingredient for the solvent—solid interface is \( \sigma_s \) and that on the free surface it is \( \tau_s \), we have,

\[
c_n(v + V) + \tau_s a' + \sigma_s(a + A) = c_{n-1}v + \tau_{n-1}(a' + a^n) + \sigma_{n-1}a
\]

(9)

where, \( a \) is the original liquid—solid interface area, \( A \) is the liquid—solid interface area after the solvent is added, \( a' \) is the solution-vapor surface area when at rest and \( a'' \) is the increase in the solution-vapor surface area when being poured.

This equation can be rewritten as

\[
c_n = c_{n-1} \left( \frac{v}{v + V} + \frac{\tau_{n-1}(a' + a^n)}{v + V} + \frac{\tau_s a'}{v + V} + \frac{\sigma_{n-1} a}{v + V} \right)
\]

\[
- \frac{\sigma_s(a + A)}{v + V}
\]

which can be written as

\[
c_n = c_{n-1}f + \tau_{n-1}^l - \tau_s^l - \sigma_{n-1}^l \alpha - \sigma_s(\alpha + \beta)
\]

(10)

where

\[
\alpha = \frac{a}{v + V}, \quad \beta = \frac{A}{v + V}, \quad \lambda = \frac{a'}{v + V}, \quad \lambda' = \frac{a' + a''}{v + V}, \quad f = \frac{v}{v + V} < 1.
\]

One may rewrite Eq. (11) as

\[
c_n = c_0 f^{n_1} + \tau_0 f^{n_1} + \left( \lambda' - f\lambda \right) \sum_{k=1}^{n-1} \tau_k f^{n-1-k} - \tau_s^l
\]

\[
+ \sigma_0 a^{n_1} + (\alpha - (\alpha + \beta)f) \sum_{k=1}^{n-1} \sigma_k f^{n-1-k}
\]

\[
- \sigma_s(\alpha + \beta)
\]

(12)

which can be solved, if the values of \( \sigma \) and \( \tau \) are known.

From the Langmuir adsorption isotherm at high dilutions as in the previous case, one gets

\[
c_n(v + V) + Qc_{n-1} + Kc_s(a + A) = c_{n-1}v + Qc_{n-1}(a' + a^n) + Kc_{n-1}a
\]

(13)
which gives
\[ c_n = c_{n-1} \left( \frac{f + Q' + K \alpha}{1 + Q' + K(\alpha + \beta)} \right) = c_{n-1} \gamma \]  
which gives
\[ c_n = c_0 \gamma^n. \]  

If \( f < (Q' + K \alpha)/(Q' + K(\alpha + \beta)) \) then \( \gamma > f \) and the dilution is slower than perceived. If one uses \( v = 1 \text{ cm}^3 \), \( V = 9 \text{ cm}^3 \), \( a = 50.8 \text{ cm}^2 \), \( A = 4.5 \text{ cm}^2 \), \( K = Q = 0.07 \) (from the data by Chang et al.\textsuperscript{15} as discussed in previous section), \( g' = 50.3 \text{ cm}^2 \), \( a'' = 0.02 \text{ cm}^2 \), \( \alpha = 5.1 \text{ cm}^{-1} \), \( \beta = 0.45 \text{ cm}^{-1} \), \( \lambda = 5.027 \text{ cm}^{-1} \), one gets \( \gamma = 0.46 \). This would imply that a 30C dilution is effectively a 9C dilution.

### Dilutions of multicomponent mixtures

For multicomponent mixtures, the effect of all surfaces would be to change the composition of the mixtures unless the equilibrium constants of the individual components are equal. If the concentration of the \( i \)th component in the \( n \)th dilution is \( c_n^i \) and the \( I \)th component in the \( n \)th dilution is \( c_n^I \). It can be seen, that for the second mixing scheme
\[ c_n' = c_{n-1}' \left( \frac{f + Q_{n} + K_I \alpha}{1 + Q_{n} + K_I(\alpha + \beta)} \right) = c_{n-1}' \gamma_I, \]  
and
\[ c_n'' = c_{n-1}'' \left( \frac{f + Q_{n} + K_H \alpha}{1 + Q_{n} + K_H(\alpha + \beta)} \right) = c_{n-1}'' \gamma_H, \]  
where the equilibrium constants are \( \sigma_n^I/c_n^I = K_I(T) \), \( \tau_n''/c_n'' = Q_H(T) \), and \( \sigma_n''/c_n'' = K_H(T) \). This gives,
\[ c_n' = c_n'' \left( \frac{\mu_I}{\mu_H} \right)^n, \]  
and for the Korsakovian scheme, it is
\[ c_n' = c_n'' \left( \frac{\gamma_I}{\gamma_H} \right)^n. \]  

Here we see that unless \( K_I = K_H \) and \( Q_I = Q_H \), the ratio of the mole fractions of the components will keep varying with successive dilutions.

Assuming \( K_I = Q_I = 0.07 \text{ cm} \) and \( K_H = Q_H = 0.026 \text{ cm} \) (along with the geometry parameters as in the previous two sections) one gets \( \mu_I/\mu_H = 0.26/0.18 = 1.44 \) and \( \gamma_I/\gamma_H = 0.46/0.28 = 1.63 \) and hence the ratio of the concentrations would evolve as given by Eqs. (18) and (19).

### Discussion

The effect of surface should be considered when calculating dilution. Here two schemes of dilutions are shown and more schemes could be envisaged (e.g., using the same lid for succussion or draining in place of pouring which would have similar mathematical ramifications).

The main thrust of this work is to show that the effect of the surface on dilution would may result in concentrations much larger than what is naively perceived. One may also note here that the equilibrium constant \( K \) would depend on the mixing container (whether it is glass, stainless steel, quartz) as different materials and different active ingredients and solvents would have different values of \( K \) and \( Q \). For multicomponent mixtures, unless the equilibrium constants are comparable, the ratio of the mole fraction of the components would keep changing with dilutions. The material of the containers also plays a role in the generation of nanoparticles.\textsuperscript{16}

A proper and accurate measurement of concentration of active ingredient is needed before considering a certain dilution beyond the Avogadro limit. The function of succussion, its role in establishing equilibrium or in the formation of nanostructures\textsuperscript{13,17,18} and conformational changes, if any, of macromolecules at large dilutions need to be understood separately.

### References

9. Private communication with Dr. Parimal Banerjee.

