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In vitro adsorption kinetic model of phenobarbital onto powdered seeds of *Garcinia kola*

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The *in vitro* adsorption kinetics of phenobarbital on *Garcinia kola* seed powder was investigated. Batch adsorption experiment to determine effects of adsorbent dose (0.1 to 2.0 g), adsorbate concentration (50 to 200 ppm), contact time (20 to 300 min) and temperature (298 to 318 K) was conducted. Adsorption data were subjected to different experimental and theoretical adsorption kinetic models (first order, second order, Elovich equation and modified Freundlich). The adsorption rate constants obtained from the best fit model were used to determine the activation energy, E_a from the Arrhenius equation. The studies showed that adsorption of phenobarbital onto powdered *G. kola* seed followed second order kinetics with adsorption rate constant (0.174 to 2.156 g mg^{-1} min^{-1}) at 298 to 318 K with good correlation coefficient (0.909 to 0.951). The adsorption equilibrium was attained after 4 h with different equilibrium concentration (0.0902, 0.0864 and 0.0968 mg/ml) at 298, 308 and 318 K, respectively. Intra-particle adsorption model revealed three stages of adsorption with different K_{iads} which implied that intra-particle diffusion could not be the only factor controlling phenobarbital adsorption onto *G. kola* seed. Arrhenius plot gave E_a of 99.435 KJ mol^{-1} and frequency factor of 5.25 × 10^{16}. In conclusion, adsorption of phenobarbital followed strictly second order kinetic model and its overdose and/or poisoning could be effectively managed with *G. kola* seed powder.

Key words: Kinetic model, adsorption, *Garcinia kola*, Arrhenius equation, phenobarbital.

INTRODUCTION

Kinetics of adsorption studies the rate (from which rate laws and specific constants are derived) of adsorption processes by investigation of how different experimental conditions can influence the speed of adsorption and provide sufficient information about the adsorption mechanisms, transition states and possible kinetic models (Ho and McKay, 2000; Siminiceanu et al., 2010; Ho and McKay, 1999; Saiers et al., 1994; Ho and McKay, 1998; McKoy and Liapis, 1991; Ho, 1995; Mohan et al., 2002; Chu and Hashim, 2003; Zeldowitsch, 1934;

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Lagergren, 1898; Zaror, 1997; O'Shannessy and Winzor, 1996) that can describe the adsorption processes. This involves understanding of relatively simple rate laws existing for zero, first, second or multi-orders of adsorption (Srivastava et al., 1997) and expe-rimentally determined activation energy using Arrhenius (Eddy et al., 2009) and Eyring-Polanyi equations (Evans and Polanyi, 1935; Eyring, 1935) and factors (adsorbate concentration, pH, catalyst, temperature, and physical state of adsorbent/adsorbate) that affect adsorption rate.

In cases of drug overdose and/or poisoning, understanding kinetics of elimination or disposition plays significant role in managing drug's untoward effects. This process is advantageous for some category of drugs, foods and cosmetics, especially those with narrow therapeutic indices. Drugs with narrow therapeutic index, such as phenobarbital, have been linked to many drug-related problems (DRPs) which are caused by patient, logistics, treatment duration, health care providers, dose selection and drug form, selection, use and administration (Bergkvist-Christensen et al., 2011). These are group of undesired patient experiences that involves drug therapy and that actually or potentially interferes with the desired patient outcome (Cipolle et al., 2004). Pharmaceutical care performs the basic function of identifying potential and real drug-related-problems, provides solution to the real DRPs and prevents potential DRPs (Helper and Strand, 1990) of barbiturate which has necessitated the common dosage titration and close monitoring always suggested in treatment guidelines for phenobarbital and related drugs.

In cases of real DRPs of phenobarbital, however, many remedies have been identified (Mohammed and Abdel-Rahman, 2001; Proudfoot et al., 2004) which themselves pose great challenges to the patient's treatment outcomes. The effective use of an agent (adsorbent) as antidote in cases of poisoning and drug overdose is governed primarily by the rate the agent arrest and hold on to the poison(s) prior to disposition or inactivation before irreversible damages occur. The phytochemical constituents (oleoresin, tannin, saponin, alkaloids, glycoside, biflavonoids) of *Garcina kola* (Adesuyi et al., 2012) have been responsible for its purgative, antiparasitic, antimicrobial, anti-inflammatory, antioxidant, antidiabetic and antispasmodic activities (Braide, 1991; Iwu et al., 1990; Leverin and Mc Matron, 1999). Experience, however has shown that adsorption potential of *G. kola* may not lie in any of the phytoconstituents but in the bulk powdered seed.

Surprisingly, there is paucity of information on the use of *G. kola* as antidote for some poisons or drug overdose (Esimone et al., 2002). More so, the processes, mechanisms and rates of such application are yet to be well elucidated. The need to use safe, locally sourced and readily available and cheap material, such as *G. kola*, as an alternative to orthodox options in manage-ment of DRPs associated with phenobarbital overdose and/or poisoning by the principles of adsorption and the kinetics, cannot be overemphasized.

MATERIALS AND METHODS

The U-2900 double beam UV-visible spectrophotometer having wavelength range of 190 to 1100 nm with 1.5 nm spectral bandpass (a product of Hitachi High-Tech Co, Japan) and the expanded memory RS232 output CyberScan pH110 pH meter -2.00 to 16.00 (Eutech, Japan) were used without re-calibration. SHZ-88 thermostatic water bath shaker, 0 to 100°C temperature controlled, 30 to 360 rpm, 0 to 120 min timing (Jintan Medical Instrument, China), magnetic stirrer with 200°C maximum heating chamber and 0 to 1000 rpm stirring speed (Remi PVT, India), laboratory water bath (Uniscope Sm801A Surgifriend medicals, England), electronic weighing balance (Adventure^{TM}, capacity 310 g, Ohaus corporation USA), vacuum pump B-42, 220V-/50-50 Hz, 5 Pa, single ¼ HP (Sigma, England), phenobarbital was a product of Vitabiotics Pharmaceuticals, Nigeria, analar methanol, hydrochloric acid and sodium hydroxide were obtained from Sigma-Aldrich, USA. The double distilled water (DDW) was procured from the distillation unit of the University of Nigeria Nsukka General Enterprises Ltd (UNGEL) Laboratory.

Preparation of *G. kola* seed powder

The freshly harvested and partially dried *G. kola* seeds purchased from a local market in Nsukka were dehulled manually, washed severally with DDW, sliced into pieces and dried in oven at temperature of 50°C for 24 h. The slices were ground, further oven dried at 70°C for 48 h and sieved. The particle sizes 1 to 2 mm were collected and stored in an air tight container prior to the studies.

Kinetics studies of phenobarbital adsorption

Phenobarbital concentration (50 to 200 ppm), adsorbent dose (0.1 to 2.0 g), sampling time (20 to 300 min), agitation speed (500 rpm) and media temperatures (25 to 45°C) were selected after preliminary batch adsorption studies. Fifty milliliter (50 ml) solution of known phenobarbital concentration was added to known amount of powdered *G. kola* seeds (GKS) in a different 200 ml measuring flasks at a definite pH (zpH of phenobarbital) at temperatures 25, 35 and 45°C with periodic agitation. At pre-determined time interval, a portion of mixture was withdrawn and filtered through the suction pump immediately to stop the adsorption and assayed spectrophotometrically. The kinetic data were fitted into empirical (Kuo and Lotse, 1974), Elovich (Chien and Clayton, 1980) and theoretical (Xiao-hong et al., 2007) models (Table 1).

Determination of activation energy

The dependence of rate constant on temperature was further

Table 1. Kinetic models investigated.

Model	Linear form of equation
First order	$In\ A = InA_0 - K_1 t$
Second order	$\frac{1}{A} = \frac{1}{A_0} + K_2 t$
Modified Freundlich	$InQ = In(KA_0) + \left(\frac{1}{m}\right) In\ t$
Elovich equation	$Q = \left(\frac{1}{\beta}\right) In(\alpha\beta) + \left(\frac{1}{\beta}\right) In\ t$

A is concentration of phenobarbital after a time t, A_0 the concentration at time t_0, Q the amount of phenobarbital adsorbed and k, m, α, β are constants.

Table 2. Adsorption kinetic parameters of phenobarbital on to GKS powder.

Models/Temperature (K)	Parameter	298	308	318
First order	K_1 (ml/min)	-0.007	-0.020	-0.017
	R^2	0.990	0.896	0.893
Second order	K_2 (g/mg min)	0.174	0.890	2.156
	R^2	0.939	0.951	0.909
Modified Freundlich	K_{ad} (ml/mg)	5.89×10^{-8}	1.51×10^{-7}	3.90×10^{-7}
	R^2	0.803	0.800	0.770
	(m)	0.3149	0.3275	0.3465
Elovich equation	α ($mgg^{-1}\ min^{-1}$)	30.303	23.256	22.727
	β ($gm\ g^{-1}$)	1.177×10^{-3}	1.819×10^{-3}	2.141×10^{-3}
	R^2	0.859	0.939	0.856

illustrated with the plots of Arrhenius equation, $K = Ae^{-Ea/RT}$, where A is the frequency factor, E_a the activation of energy (in KJ mol^{-1}) for the adsorption, K the rate constant, $e^{-Ea/RT}$ the small fraction of the total number of collisions of *G. kola* seed powder with phenobarbital that resulted in successful adsorption, R the universal gas constant (8.314 $JK^{-1}\ mol^{-1}$) and T absolute temperature (in K). Figure 4 shows the linear plot of In K_{ads} vs 1/T (K^{-1}). The E_a is determined from the slope ($-E_a/R$) and A from intercept (In A) on vertical axis (Cairns, 2008).

Phenobarbital assay

All assays of phenobarbital concentrations were based on pre-validated standard calibration method by UV spectrophotometric measurement of absorbances at maximum absorption wavelength of 284 nm for phenobarbital 0.5 to 20 ppm with coefficients of variation less than 2% both intra- and inter day. For each measurement, appropriate blanks were selected to match the signal from the sample cell with that of the reference cell of the spectrophotometer. All determinations were carried out in triplicate.

RESULTS AND DISCUSSION

The results of the studies are presented in Figures 1 to 4 and Table 2. The results of effects of contact time showed that the amount of phenobarbital adsorbed onto GKS increased progressively with the time and temperature rise. This confirms the findings of Nnadi et al. (2014)

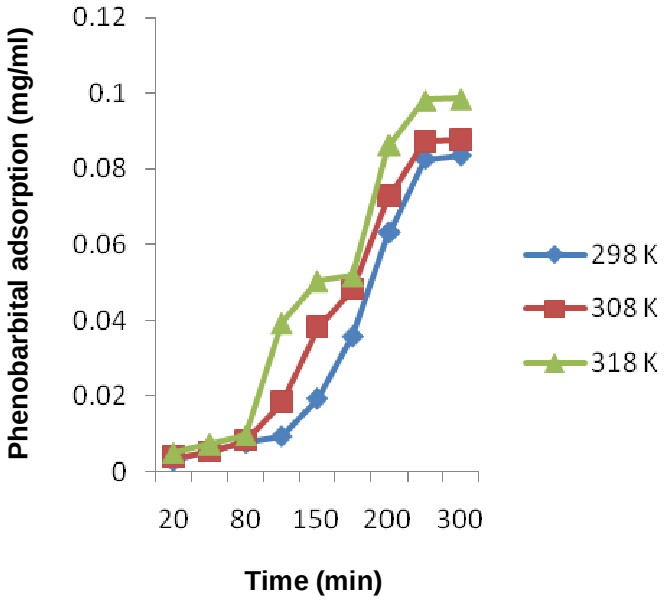

Figure 1. Effect of contact time on phenobarbital adsorption at 25 to 45°C (adsorbent 1.00 g, phenobarbital 100 µg/ml, pH 7.10).

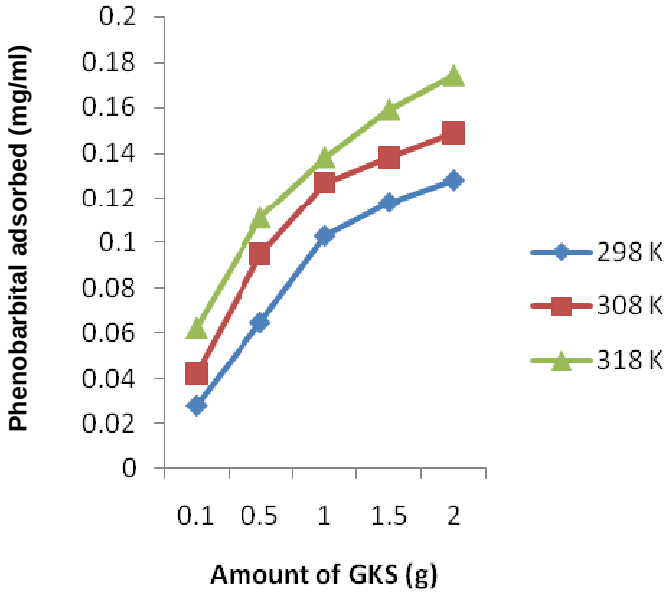

Figure 2. Effect of adsorbent dose at 25 to 45°C (phenobarbital 200 µg/ml, pH 7.10, time 5 h).

that the adsorption process is endothermic in nature. This is probably due to larger surface area of GKS available at the onset for the adsorption of pheno-barbital. Figure 1 shows that about 240 min is enough for the system to attain equilibrium at different temperatures (298, 308 and 318 K) corresponding to equilibrium concentration of 0.0902, 0.0864 and 0.0968 mg/ml, respectively. Similar trends were observed in previous reports as a result of increased diffusion of drug molecules into the internal porous structure of adsorbent surfaces (Suteu and Bilba, 2005; Zaker et al., 2013). Beyond the equilibrium time, however, the concentration gradient decreases due to the increased occupation of the active adsorption sites by the drug molecules (Jiwalak et al., 2010).

The results of adsorbent dose effect on phenobarbital adsorption showed that the amount of phenobarbital adsorbed increased significantly as the adsorbent dose increased from 0.1 to 2.0 g. Similar trends were observed by previous researchers (Awala and El Jamal, 2011; Al-Bayati and Ahmed, 2011). This could be attributed to increased sites of adsorption provided by additional adsorbent for every weight increase, enhanced interaction between GKS and phenobarbital, increased necessary driving force to counter resistance to mass transfer and confirms adsorbent dose significant factor in adsorption (Suteu and Bilba, 2005). Another factor that contributed to the increased adsorption rate is the porosity of the powdered GKS. Previous findings (Seichi et al., 2005; Binary and Narenda, 1994; Annadurai and Krishnan, 1997) identified complex adsorption processes of three theoretical elementary stages for porous materials under isothermal condition represented by the diffusion of the drug molecules into fluid film (film diffusion), diffusion of drug molecules into the capillaries and on to the surfaces of the adsorbent (internal diffusion) and finally the adsorption of drug molecules on the corresponding active and specific sites of the adsorbent (sorption). The overall rate, considering the complexity of the process, is governed by the corresponding rates of the three elementary processes, which the practicability has not been clearly resolved or by the rate of the fastest process; the rate-determining step (Boyd et al., 1947).

The applications of different kinetic models to adsorption data were shown in Figure 3, and their kinetic parameters in Table 2. The conformity of the experimental adsorption data with different models tested was expressed in terms of R^2 values. High R^2 values (>> 0.9) indicated successful model, however, high values (< 0.9) does not always indicate best model (Kithome et al., 1998).

The results showed that adsorption of phenobarbital on GKS followed theoretical second order kinetics only with R^2 values 0.909 to 0.951 at temperatures 298 to 318 K. This fact suggests that phenobarbital adsorption on to

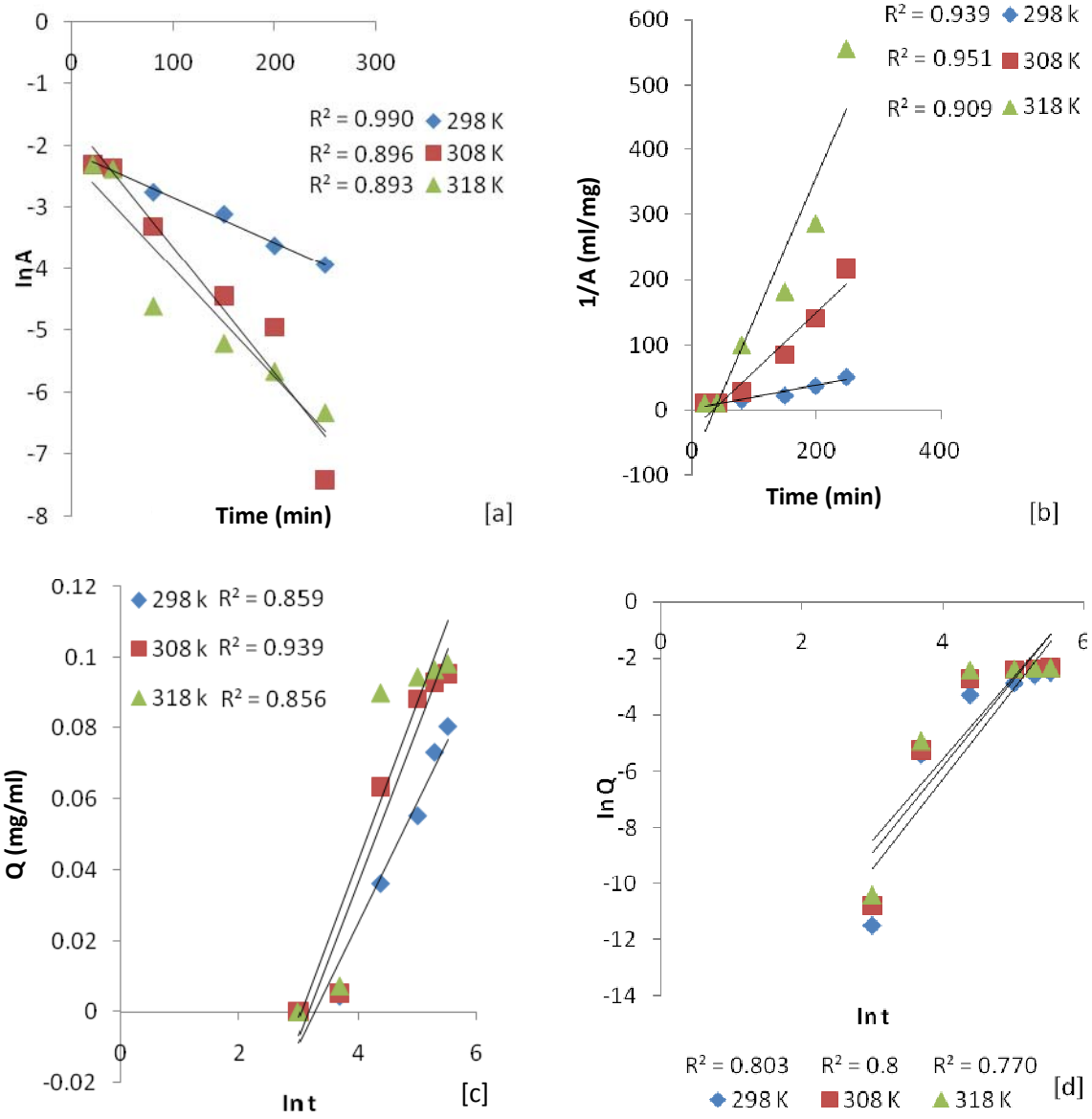

Figure 3. Kinetic models investigated-(a) First order, (b) second order, (c) Elovich equation, (d) Modified Freundlich plots.

GKS relies on the assumption that chemical adsorption may be the rate-limiting step. In this case, the drug sticks to the adsorbent surface by forming a covalent bond and tends to find sites that maximize its coordination number with the surface (Wong et al., 2003). However, significant parameters were also obtained from other models examined. The Elovich adsorption model showed that the initial adsorption rate (α) reduced from 30.303 to 22.727 mg/g min as the temperature increased while the desorption constant (β) increased linearly with the temperature from 1.177×10^{-3} to 2.141×10^{-3} g/mg. The higher values of adsorption rate compared to desorption at all temperature showed the feasibility of the use of *G. kola* seed in management of barbiturate-related overdose and/or poisoning especially at low temperature where adsorption >>> desorption eventhough previous reports (Sparks, 1989) had indicated that the chemical significance of these constants (α and β) were yet to be evaluated.

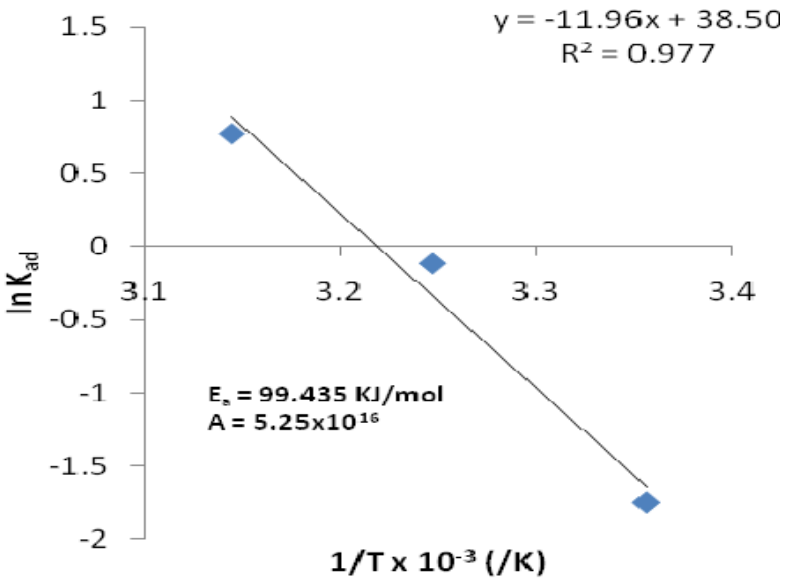

Figure 4. Arrhenius plot of second order adsorption kinetics.

However, physical and experimental parameters significant to phenobarbital adsorption were also obtained from the first-order and modified Freundlich kinetics models though the models did not provide valid correlation coefficients ($R^2 \geq 0.9$) required to ascertain their relevance in this study with the exception of first order model at 298 K ($R^2 = 0.990$) and Elovich model at 308 K ($R^2 = 939$) (Table 2).

In order to further understand the kinetic mechanism of adsorption, intra-particle diffusion model (Ho and McKay, 1998) was applied to the adsorption data (plots not shown for purpose of brevity) by plotting Q_t against $t^{0.5}$. The plot indicated that three stages in the adsorption processes existed, representing the influence of external membrane diffusion of drug (boundary layer diffusion that slows adsorption), gradual adsorption stage (intra-particle diffusion) and adsorption equilibrium, respectively suggesting that intra-particle diffusion could not be the only factor driving adsorption in this study. The study further revealed that possibly kinetic mechanism could be governed by two-dimensional diffusion, chemical ion exchange, chemical displacement and/or mass transfer processes depending on which of them was the rate limiting step (Kithome et al., 1998).

The specific constant of the second order adsorption increased (0.174 to 2.156 g mg^{-1} min^{-1}) linearly with temperature. The results showed that activation energy of adsorption was relatively low (99.435 KJ/mol) compared to activation energy of organic and inorganic reaction and with high frequency factor (Figure 4) which confirms the feasibility of the adsorption process. Theoretically, the value of E_a may give an indication of whether chemisorption or physisorption process is in operation. As a result of easily reversible interaction in physical adsorption, its energy requirements are usually so small that E_a lies within 5 to 40 KJ/mol while the much stronger bonding forces in chemisorption demands higher E_a of 40-800 KJ/mol (Nollet et al., 2003) which further confirmed the earlier findings of chemical adsorption process in this study.

The successful application of Arrhenius equation, in this case, is dependent on the assumptions that the linearity of the plot (Figure 4) obtained from the Arrhenius equation extends to room temperature (in other words, A and E_a are independent of temperature) and that the same mechanism controls adsorption of phenobarbital onto GKS at both temperature extremes (Cairns, 2008).

Conclusion

G. kola seed powder can be efficiently used for the management of phenobarbital poisoning or overdose by principles of adsorption. The adsorption increases linearly with phenobarbital concentration, temperature and adsorbent dose. The adsorption follows second order kinetic model and the mechanism was also found to obey intra-particle diffusion model.

Conflict of interest

Authors declare that they have no competing interests.

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