Abstract

Introduction

Occurrence of soluble pharmaceutically important compounds in plant products is abundant but their separation and purification particularly in maintaining the original value and also minimizing the residual effects because of predominant use of various chemical extraction methods is often difficult\(^1\). Separation of pharmaceutically important plant products and their need of study to explore new purification methods to overcome the problems are discussed. Two pharmaceutically significant water soluble plant products viz. caffeine and ginsenoside are selected and taken as standard representative compounds for undertaking the present study. An adsorptive separation technique, which is based on polymeric resins, is used as a potential solution to the separation difficulty.

The objective of the research work is to study the equilibrium, kinetics and enthalpies of aqueous phase adsorption of certain pharmaceutically important bioactive compounds with selected neutral polymeric resins for suggesting appropriate isotherm and kinetic model. The study is also projected to develop a knowledge base for design of suitable adsorbents with high selectivity and capacity for the selected pharmaceutically important biomolecules like caffeine and ginsenoside through experimental studies and establish the feasibility of the adsorptive separation process in fixed bed columns to suggest appropriate configuration for design of process through mathematical modeling and simulation exercises in technological perspectives.
The structure and properties of the selected compounds along with those of the polymeric resins and their advantage of use in separation and purification processes are presented and discussed. An overview of the adsorptive separation process and its significance and importance with reference to separation and purification of high valued plant products from aqueous solutions is also provided.

**Adsorption equilibrium**

The fundamental aspects of study for assessing the feasibility of an adsorption process for practical application including the theoretical phenomena involved in the adsorptive separation process are discussed. The adsorption behaviour of caffeine and ginsenoside from aqueous solution onto polymeric resins such as XAD-4, XAD-7, XAD-16 and XAD-1180 was studied. Adsorption isotherms were interpreted from various isotherm models like Langmuir, Freundlich, Redlich–Peterson, Dubinin–Radushkevich and Temkin and their parameters were evaluated and compared. The removal effectiveness of ginsenoside onto the studied resins was found to be in the order of XAD-7 > XAD-16 > XAD-1180 > XAD-4 and the equilibrium sorption was achieved in about 6 hours. The adsorption efficiency and uptake rates of caffeine onto various resins were compared and the highest adsorption efficiency was observed with the poly-aromatic neutral resins XAD-4 and XAD-16. The adsorption efficiency and uptake rates of ginsenoside onto various resins were also compared and the highest adsorption efficiency and rate were observed with Amberlite XAD-7 resins. The optimum adsorbent doses for all the adsorbents were found to be 10–15 g L\(^{-1}\) with uniform adsorption at a concentration of 0.33 g L\(^{-1}\) ginsenoside. Five different isotherm models provided by Langmuir\(^1\), Freundlich\(^2\), Redlich-Peterson\(^3\),
Dubinin-Radushkevich and Temkin were used to fit the experimental equilibrium data for sorption of aqueous ginsenoside onto four different polymeric adsorbents, XAD-4, 7, 16 and 1180. The observed profiles of solid phase concentration of ginsenoside at equilibrium, onto the resins against the liquid phase concentration $C_e$, indicate a good fit for the models except the Dubinin-Radushkevich model to the experimental data verifying that the adsorption processes are favourable. The mean free energy of adsorption for ginsenoside was estimated using the Polanyi Potentiali and the D-R isotherm constants and were in the range of 0.04–0.26 kJ mol$^{-1}$ signifying occurrence of physical adsorption. For the adsorption of caffeine, the adsorption isotherms were interpreted on three different neutral polymeric resins viz. Amberlite XAD-4, XAD-7 and XAD-16 at 298 K. The experimental data were well fitted to the Langmuir and Freundlich isotherm in the studied concentration range. Amberlite XAD-4 and XAD-16 were observed to have better adsorption efficiency than that of XAD-7 resin for caffeine adsorption.

Adsorption kinetics

The kinetics study of removal of ginsenosides and caffeine from aqueous solutions on polymeric Amberlite adsorbents were carried out by batch adsorption technique. The factors affecting the rate processes involved in the removal of ginsenosides and caffeine at different initial concentrations, agitation speed, mass of adsorbent and temperature, have been studied. The adsorption kinetics for caffeine onto different amberlite resins was analyzed from a first order rate process and the first order rate constant values ($k_{ad}$) were found to vary in the order $k_{ad(XAD-4)} > k_{ad(XAD-16)} > k_{ad(XAD-7)}$. The adsorption efficiency and uptake rates of caffeine onto
various resins were compared and the highest adsorption efficiency was observed with the poly-aromatic neutral resins XAD-4 and XAD-16. The first order rate expression well represents the caffeine adsorption process onto XAD-4 and XAD-16. The data of caffeine adsorption onto XAD-7 resin generally fit the Lagergren equation. The adsorption kinetics for ginsenoside was analyzed using series of rate equations like first-order rate equation, second-order rate equation, Bangham’s model, Intra-particle diffusion model, Boyd’s diffusivity model and Elovich kinetic equation. It is observed that the ginsenoside adsorption process follows pseudo second order rate kinetics, corroborating high correlation coefficients for calculated parameters with the experimental data. The ginsenoside adsorption study also reveals that the diffusion of the adsorbate into the pores is not the only rate controlling step but both film and pore-diffusion play significant role to different extent and stages of contact in the sorption process. XAD-7 has significant influence of external mass transfer effect in the adsorption process of ginsenoside.

**Adsorption thermodynamics**

The present study is also projected to determine the basic thermodynamic parameters of ginsenoside and caffeine adsorption in aqueous media in order to improve current understanding of adsorption phenomena occurring in the process. Based on their efficiency of uptake carried out in the batch equilibrium study, the effect of temperature on adsorption of ginsenoside on polymeric adsorbents was studied on two of the adsorbents, XAD-7 and XAD-16. The adsorption performance was investigated thermodynamically under batch equilibrium conditions at 293, 298, 303 and 308 K. It is observed that temperature has a distinct effect on the adsorption
capacity of the adsorbents. The optimum temperature of adsorption was observed to be 298 K. for both the resins in the adsorption process. It is observed that at lower adsorbate concentrations, the solute uptake increases sharply and beyond 298 K the adsorptivity decreases with increase in temperature.

The isotherm parameters for three different isotherm models viz. Langmuir, Freundlich and Temkin models at different temperatures for ginsenoside adsorption onto XAD-7 and XAD-16 are presented. It is observed that Temkin and Freundlich models best fit the experimental adsorption data for XAD-7 and XAD-16 resins and 298K is the most preferred temperature for adsorption.

Adsorption thermodynamic parameters were obtained from adsorption equilibrium constants with temperatures using thermodynamic equations available in literatures\textsuperscript{13-15}. The estimated values of the thermodynamic parameters for the operating temperatures are presented. The negative values of $\Delta G^0$ confirm feasibility of ginsenoside adsorption onto XAD-7 and XAD-16 surfaces and the negative values of $\Delta S^0$ indicate non-spontaneity of the adsorption process. Negative value of $\Delta H^0$ designates the adsorption process to be exothermic in nature.

The adsorption performance of caffeine was also investigated thermodynamically under batch equilibrium experimental conditions at three different temperatures of 298, 308 and 318 K. The uptake of caffeine decreases with temperature and the optimum temperature of adsorption was observed to be 298 K. The changes in adsorption enthalpy, entropy and free energy investigated. The estimated values of the adsorption enthalpy, free energy changes and changes in entropy indicate the feasibility and spontaneity of the adsorption process. Amberlite
XAD-4 and XAD-16 were observed to have better adsorption efficiency than that of XAD-7 resin. It is observed that the uptake of caffeine decreased with increasing temperature at the adsorption time of contact. Negative values of the adsorption enthalpy indicate the adsorption process to be exothermic\(^\text{16}\). 

*Column dynamics*

Extensive studies have been made on the adsorption of various bio-molecules on neutral polymeric resins\(^\text{17-20}\). There is, of course, no hint in the literature of the application and effectiveness of Amberlite polymeric adsorbents in the separation of ginsenosides from aqueous solutions of ginseng extracts except this present research and the publications made thereof\(^\text{21}\).

Adsorption columns closely simulate commercial and industrial adsorption systems. The adsorption column, or contactor, separates bio-molecules in the feed stream provided there is sufficient contact time between the solute in the aqueous phase of the bulk liquid and the adsorbent\(^\text{22, 23}\). The column dynamics study for adsorption of ginsenoside from aqueous solution was undertaken in fabricated fixed bed experimental columns. The operating conditions for the best result of the batch equilibrium studies for adsorption of ginsenoside on selected polymeric adsorbents were adopted for the column dynamics studies. Break-through curves were generated in the experimental fixed bed columns at varying flow rates in the range of 1 to 5 ml/min. The best performance was recorded at a flow rate of 2.5 ml/min in a column of 300 mm length with 10 mm dia.
Micro transport of the solute in reality controls the sorption process by movement through the pores of the adsorbent. The mechanism is diffusion through the liquid film or external boundary layer, diffusion through the porous particle resulting in adsorption on the interior surface, and a combination of both these steps. The following continuity equation for mass balance over a section of ginsenoside deposit on the disk element considering convection diffusion for a single solute is taken as a model for theoretical solution and comparison with the experimental conditions and results:

\[
\frac{\partial^2 C}{\partial z^2} - \frac{v}{\epsilon} \frac{\partial C}{\partial z} = \frac{\partial C}{\partial t} + \frac{(1 - \epsilon)}{\epsilon} \frac{\partial q}{\partial t}
\]

where, \( \frac{\partial q}{\partial t} \) represents the mass transfer rate of the solute to the adsorbent bed and \( \frac{\partial C}{\partial z} \) is the variation of concentration along the axial direction of the column. \( D_L \) is the axial dispersion coefficient and \( \epsilon \) is the bed porosity. The axial diffusion and mixing at the exit of the deposit is determined through solving the equation by taking Dancwart’s boundary conditions. The approach has been programmed into MATLAB script where, systems of partial differential equations and their associated boundary and initial conditions were entered and solved over a domain that has been discretized by user-defined meshes. Numerical computation exercises were carried out and the partial differential equation is solved by using MATLAB 2008b (Math Works Inc., USA) pdepe solver to predict the dimensionless ginsenoside concentration, \( C^* = C/C_0 \) in the column across the macro porous Amberlite XAD-7 resin packed bed with reference to the dimensionless time, \( \tau = t/T \) of column operation. Plot of theoretical model with that of experimental results for set of data
generated at 2.5 ml/min flow rate in the column adsorption is presented. The solution plot depicts that the initial rate of ginsenoside uptake by the resins and the overall trend of attaining equilibrium is comparable to that of the theoretical model.

The distribution of concentration inside the spherical resin particles in the radial direction inside the experimental adsorption column is also determined theoretically by using the following equation:

$$\varepsilon_p \frac{\partial C}{\partial t} + (1 - \varepsilon_p) \frac{\partial q}{\partial t} = D_e \left( \frac{\partial^2 C}{\partial r^2} + \frac{2}{r} \frac{\partial C}{\partial r} \right)$$

where, $r$ is the radial ordinate and $R$ is the particle radius. $\frac{\partial q}{\partial t}$ is the rate of mass transfer of solute and $\frac{\partial c}{\partial r}$ is the change in concentration along radial direction. $\frac{\partial c}{\partial t}$ represents the rate of change in liquid phase concentration. The effective pore diffusivity $D_e$ is related to the external mass transfer coefficient $k_f$ in the boundary condition at $r = R$. The correlations developed by many researchers for estimation of the external mass transfer coefficient $k_f$ are discussed and the most accepted basic correlation developed by Ranz and Marshal\textsuperscript{24} is adopted for solving the partial differential equation using dimensionless groups over the domain of the boundary conditions in the radial direction of adsorption. The solution of the model using MATLAB 	extit{pdepe} solver generate surf plot of distribution of ginsenoside concentration at various radial length inside the column against the time of column operation.

It can be concluded from the column dynamic study conducted that Amberlite XAD-7 polymeric resins could be successfully used for separation of ginsenoside from aqueous solution. The equilibrium time for adsorption on the adsorbate bed is
around 2h. The maximum adsorption capacity is 27.9 mg g\(^{-1}\) of resin at an optimum flow rate of 2.5 ml min\(^{-1}\) for the column under study indicating more than 90% separation. The adsorption capacity is strongly dependent on the flow rate of the solution across the bed. The theoretical solid diffusion control model describing the single solute adsorption in a fixed bed based on the linear driving force kinetic model was successfully applied to investigate the adsorption of ginsenoside onto the XAD-7 resin bed. The assumptions of the model were reasonably fulfilled between the model prediction and the experimental results.

The adsorption equilibrium, kinetics, thermodynamic and column dynamic studies made in the present research work can be expected to generate technological knowledge bases for adsorptive separation as an attractive method for separation and purification of pharmaceutically important biomolecules like caffeine and ginsenoside and also down-stream processing of secondary metabolite from plant cell cultures in technological perspectives.

References


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