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Studies on the Use of Tea Leaves as Pharmaceutical Adsorbent

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Abstract: In the present research an attempt has been made to explore the possibility of using tea leaves as pharmaceutical adsorbent. Adsorption of cefotaxime sodium (CS), paracetamol (Para), caffeine (Caf), Chlorpromazine hydrochloride (Cpz) and metronidazole (Metro) on tea leaves has been studied under different experimental conditions. The maximum adsorption capacity was observed for chlorpromazine HCl and cefotaxime sodium followed by caffeine and paracetamol. Least adsorption capacity was observed for metronidazole. It is seen that 179-457 mg of various drugs could be adsorbed per gram tea leaves at 25°C and pH 7.4. Adsorption data was found to obey both Langmuir and Freundlich adsorption isotherms. The adsorption capacity of all the drugs increased with increase in pH indicating thereby that negatively charged and neutral species are preferentially adsorbed by tea leaves as the pH is increased. At the highest pH used, 181-631 mg of drugs could be adsorbed per g tea leaves. The adsorption was fairly rapid, 80-90% of adsorption occurred in the first 3-4 h in most cases. The amount adsorbed decreased with increase in temperature in each case and the enthalpy of adsorption was found to be in the range -8.732 to -11.765 kJ mol^{-1}. The weight of tea leaves required per dose for the commonly used doses of these drugs was also calculated. Tea leaves were found to be good adsorbents for these drugs and the data can be explored for the design of drug delivery systems as well as use of tea leaves as safe, natural and effective antidote for these drugs. The results were specially significant in the case of antipsychotic drug, chlorpromazine hydrochloride, where only 0.06 g tea leaves are required per dose and therefore, tea leaves are an excellent adsorbent for this drug. The present study leads to an important conclusion that tea leaves have the potential to be used as a safe and effective pharmaceutical adsorbent for the studied drugs.

Key words: Adsorption, tea leaves, drugs, pharmaceutical adsorbent

INTRODUCTION

Tea (*Camellia sinensis*) is a tropical evergreen shrub. Black, green and oolong are considered to be the basic types of tea. Black tea, prepared from green tea leaves that have been allowed to oxidize, is the most common form of tea worldwide. All tea leaves contain four basic types of constituents: vitamins, essential oils, polyphenols and caffeine (Hara, 2001). Aside from water, tea is the most widely consumed beverage in the world. Current research has shown that tea contains specific antioxidants and health promoting ingredients (Higdon and Frei, 2003), lowering the risk of heart disease (Davies *et al.*, 2003), stroke (Ikeda *et al.*, 2007) and certain types of cancer like oral, pancreatic and prostate (Mukhtar and Ahmad, 2000). Green tea has also been reported to have antidiabetic properties; it enhances insulin activity and the predominant active ingredient is epigallocatechin gallate (Anderson and Polansky, 2002). Most of the work reported in the literature refers to the medicinal uses of tea and tea extract. However, in the present study it was thought of interest to explore the

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possibility of using tea leaves as pharmaceutical adsorbent. Tea leaves, being natural, biodegradable, non-toxic, easily available and cost effective, offer a number of advantages over other drug carriers. Drug delivery through medicated tea and use of tea leaves as antidote for drugs has not been reported before. Adsorption of a wide range of drugs on tea leaves has been studied under different experimental conditions using ultraviolet absorption spectroscopic technique for drug analysis.

MATERIALS AND METHODS

Materials
Drugs

Cefotaxime sodium (CS), paracetamol (Para), caffeine (Caf), chlorpromazine hydrochloride (Cpz) and metronidazole (Metro) were obtained as gift samples from various manufacturers. Black dried tea leaves were procured locally. All other reagents were of analytical grade and were used without further purification. Water used was double distilled in an all glass apparatus. 0.1M phosphate buffer of pH 7.4 was prepared by mixing 19 mL of 0.2M NaH_2PO_4 with 81 mL of 0.2 M Na_2HPO_4 and diluting the mixture to 200 mL with water. In the pH range 2-10, 0.1M Na_2HPO_4-HCl/NaOH buffers were used.

Drug Analysis

Ultraviolet absorption spectroscopic technique was used for drug analysis. Phosphate buffer was used as solvent. Since buffer could extract active constituents of tea leaves which adsorbed in the UV range (270 nm), extinction coefficients of all the drugs were determined in phosphate buffer containing tea extract, prepared by mixing 0.001 g tea leaves with 10 mL buffer for 24 h. All absorbance data was corrected for the absorbance of tea extract.

Adsorption of Drugs on Tea Leaves

For studying the adsorption of drugs on tea leaves, 1 mg of tea leaves were mixed with 10 mL of drug solutions of increasing concentrations prepared in 0.1M phosphate buffer (pH 7.4). The contents were mixed and allowed to stand at 25°C for 24 h for attainment of adsorption equilibrium. The tea leaves were removed by filtration and the filtrate was analysed for drug concentration by ultraviolet absorption spectroscopic technique after appropriate dilution. The initial drug concentration (C_i) was varied from 50-2000 µM. The drug concentration at equilibrium was calculated as $C_e = \{(A-A_{TE}) \times$ dilution factor$\}/\varepsilon$, where A and A_{TE} are the absorbance of drug solution and tea extract, respectively and ε is the molar extinction coefficient of the drug. The amount of drug adsorbed per gram tea leaves (x/m) was calculated as x/m (mg g^{-1}) = $[(C_i - C_e) \times 10^{-3} \times MW \times 10]/1000$ w, where 10 is the volume of drug solution taken for adsorption and w, the weight of tea leaves was 0.001g in each case. To study the effect of pH on drug adsorption, concentration and temperature were kept fixed at 1000 µM and 25°C, respectively and pH was varied from 2-10 using 0.1M Na_2HPO_4-HCl/NaOH buffer. Kinetics of adsorption was studied at pH 7.4 and 25°C, keeping drug concentration at 1000 µM. The rate of adsorption, d(x/m)/dt, was calculated at 3 h time period. Experiments were also carried out at 37°C for 1000 µM drug at pH 7.4. Enthalpy of adsorption (ΔH) was calculated using modified form of Van't Hoff equation, ln $\{(x/m)_2/(x/m)_1\} = \Delta H/R \{(T_2-T_1)/ T_2\}$. The study was conducted in the department of chemistry, Panjab University, Chandigarh, India during the year 2006.

RESULTS AND DISCUSSION

Adsorption of an antibiotic (cefotaxime sodium), analgesic and antipyretic drug (paracetamol), central nervous system stimulant (caffeine), antipsychotic drug (chlorpromazine HCl) and anti-infective drug (metronidazole) on tea leaves has been studied. Extinction coefficients of various

drugs in phosphate buffer (pH 7.4) containing tea extract (0.001 g/10 mL) at the respective λ_{max} values are recorded in Table 1. The amount adsorbed (x/m) versus C_e plots for the adsorption of various drugs on tea leaves at 25°C are shown in Fig. 1. All the drugs could be adsorbed on tea leaves and the adsorption was found to be monomolecular (Type I). The maximum adsorption capacity was observed for chlorpromazine HCl and cefotaxime sodium followed by caffeine and paracetamol. Least adsorption capacity was observed for metronidazole. It is seen that at the highest drug concentration used, 179-457 mg of various drugs could be adsorbed per gram tea leaves at 25°C. Thus tea leaves are good adsorbents for these drugs. Cefotaxime sodium and paracetamol are acidic drugs with pK_a values 3.4 and 9.7, respectively. Chlorpromazine hydrochloride, metronidazole and caffeine are predominantly basic drugs with pK_a values 9.3, 2.6 and 3.6, respectively. Accordingly at pH 7.4, cefotaxime sodium and chlorpromazine hydrochloride are fully ionized whereas the other three drugs exist in predominantly unionized form. Therefore, at this pH, acidic drug, cefotaxime sodium is negatively charged, basic drug chlorpromazine hydrochloride is positively charged while other three drugs are neutral. Hence at near neutral pH, cationic, anionic as well as neutral species have high affinity for the tea surface.

Adsorption data was found to obey both Langmuir (x/m = $abC_e/(1+bC_e)$, where a and b are constants) and Freundlich (x/m = K $C_e^{1/n}$, where K and n are constants) adsorption isotherms. Constants of the Langmuir and Freundlich isotherms, obtained from their linearized forms are given in Table 2 for various drugs. Constant 'a' of Langmuir adsorption isotherm is a measure of the adsorptive capacity of the adsorbent for the adsorbate under examination and 'b' is a constant related to the enthalpy of adsorption (Florence and Attwood, 1998). Constant 1/n of the Freundlich adsorption isotherm is a dimensionless parameter related to the intensity of adsorption (Florence and Attwood, 1998).

Effect of pH

Adsorption data was also obtained at different pH values varying from 2-10 at 1000 μM drug concentration and 25°C. x/m versus pH plots for different drugs are shown in Fig. 2. The extent of

Table 1: Extinction coefficients of various drugs

Drug	λ_{max} (nm)	Extinction coefficient* (ε) $(\mu M)^{-1} cm^{-1}$
Cefotaxime sodium	233	0.0164
Paracetamol	241	0.0105
Caffeine	272	0.0086
Chlorpromazine HCl	254	0.0324
Metronidazole	320	0.0091

*Extinction coefficients have been determined in phosphate buffer (pH 7.4) containing tea extract (0.001 g/10 mL)
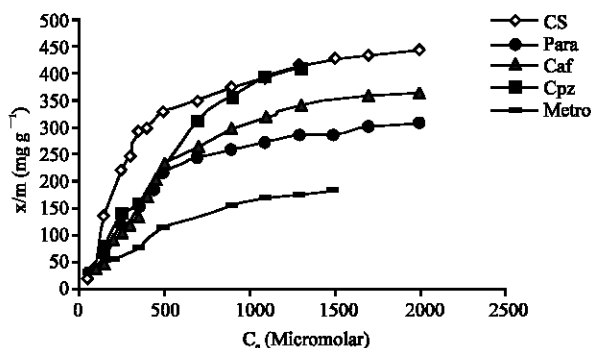

Fig. 1: Adsorption isotherms for various drugs

Table 2: Adsorption parameters for Langmuir and Friendlich adsorption isotherms

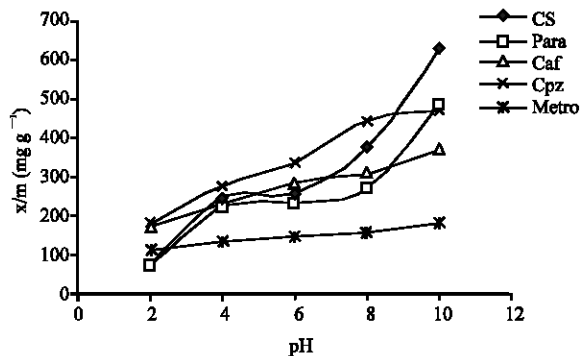| Drug	Langmuir adsorption isotherm parameters		Freundlich adsorption isotherm parameters	
	a (mg g^{-1})	b $\times 10^{-3}$(L mol^{-1})	n	log K
Cefotaxime sodium	500	3.746	3.465	1.720
Paracetamol	400	2.152	1.535	0.526
Caffeine	435	2.861	1.673	0.702
Chlorpromazine HCl	667	1.759	1.206	0.165
Metronidazole	278	1.374	1.923	0.646

Fig. 2: Effect of pH on the adsorption of different drugs on tea leaves

adsorption was found to increase with increase in pH in the case of all the drugs. However, the increase was much larger in the case of acidic drugs as compared to the basic drugs. With increase in pH, the acidic drugs (cefotaxime sodium and paracetamol) should become more and more negatively charged and therefore, it may be concluded that negatively charged species are preferentially adsorbed by tea leaves as the pH is increased. Basic drugs (chlorpromazine hydrochloride, caffeine and metronidazole), on the other hand, should become neutral as the pH is increased. Since adsorption capacity of basic drugs also increases with increase in pH, although the increase is smaller, it appears that the tea surface has some preference for neutral species as well, as the pH is increased. At the highest pH used, 181-631 mg of drugs could be adsorbed per gram tea leaves. Thus tea leaves are better adsorbents at higher pH values.

Effect of Time

To study the kinetics of adsorption process, the amount of drug adsorbed at different time intervals was determined. The concentration of drug was kept fixed at 1000 µM and the temperature was maintained at 25°C. The tea leaves were found to have high affinity for the drugs since the adsorption was fairly rapid. 80-90% of adsorption occurred in the first 3-4 h in most cases. In order to compare the affinity of different drugs for the tea surface, rate of adsorption at 3 h was calculated (Table 3). The rate of adsorption of chlorpromazine hydrochloride and cefotaxime sodium was found to be nearly three times higher than the other three drugs. Thus these two drugs have high affinity for tea surface since the adsorption capacity as well as adsorption rate are large.

Effect of Temperature

The adsorption data for various drugs at 1000 µM drug concentration and pH 7.4 was also determined at two different temperatures. The amount of drug adsorbed (x/m) at room temperature (25°C) and physiological temperature (37°C) is given in Table 3. The amount adsorbed decreased with increase in temperature in each case. This is expected since adsorption is an exothermic process. The enthalpy of adsorption was found to lie in the range -8.723 to -11.765 kJ mol^{-1} (Table 3).

Table 3: Effect of time and temperature on adsorption of drugs by tea leaves

Drug	Rate of adsorption (mg g^{-1} h^{-1})	x/m (mg g^{-1})* 25°C	x/m (mg g^{-1})* 37°C	Enthalpy of adsorption (kJ mol^{-1})
Cefotaxime sodium	154.33	380	320	-11.001
Paracetamol	51.67	265	227	-9.908
Caffeine	49.67	309	262	-10.562
Chlorpromazine HCl	155.00	411	342	-11.765
Metronidazole	55.02	157	137	-8.723

* At 1000 µM initial drug concentration

Table 4: Amount adsorbed (x/m) and tea leaves required per dose for various drugs

Drug	x/m (mg g^{-1})* pH 7.4	x/m (mg g^{-1})* pH 10	Dose** (mg)	Tea leaves required/dose (g) pH 7.4	Tea leaves required/dose (g) pH 10
Cefotaxime sodium	380	631	500	1.316	0.792
Paracetamol	265	489	500	1.887	1.022
Caffeine	309	370	200	0.647	0.540
Chlorpromazine HCl	411	424	25	0.061	0.059
Metronidazole	157	181	200	1.274	1.105

*Reported x/m values are at 1000 µM initial drug concentration. ** Commonly used doses of various drugs are mentioned

Pharmaceutical Applications

An attempt has also been made to explore the possible pharmaceutical applications of the adsorption results discussed above. The amount adsorbed (x/m) at 1000 µM initial drug concentration and the weight of tea leaves required per dose for various drugs at pH 7.4 and 10 are given in Table 4. It is seen that for the commonly used doses, a very small quantity of tea leaves (0.061-1.887 g at pH 7.4 and 0.059-1.105 g at pH 10) are required per dose. Thus tea leaves are good adsorbents for all the drugs. These adsorption characteristics can be explored for the design of drug delivery systems as well as use of tea leaves as safe, natural and effective antidote for these drugs.

The results are specially significant in the case of antipsychotic drug, chlorpromazine hydrochloride, where the dose required is much smaller (25 mg) and the adsorptive capacity is high. Thus only 0.06 g is required per dose and therefore, tea leaves are an excellent adsorbent for this drug. The toxicity of antipsychotic and antidepressant drugs due to overdose or accidental intake is commonly encountered (James and Kearns, 1995). Thus tea leaves can be used as safe antidote for chlorpromazine hydrochloride with no side effects.

CONCLUSIONS

The adsorption was found to be monomolecular and at the highest drug concentration used, the adsorptive capacity at 25°C was in the range 179-457 mg g^{-1} tea leaves at pH 7.4. The adsorptive capacity increased with increase in pH. At the highest pH studied, 181-631 mg of drugs could be adsorbed per gram tea leaves. Adsorption was fairly rapid, 80-90% adsorption occurred in 3-4 h. The enthalpy of adsorption was in the range -8.723 to -11.765 kJ mol^{-1}. The weight of tea leaves required per dose for the commonly used doses of these drugs was found to be 0.061-1.887 g at pH 7.4 and 0.059-1.105 g at pH 10. A small quantity of tea leaves required per dose showed that tea leaves are good adsorbents for these drugs and the data can be explored for the design of drug delivery systems as well as use of tea leaves as safe, natural and effective antidote for these drugs. The results are specially significant in the case of antipsychotic drug, chlorpromazine hydrochloride, where the dose required is much smaller (25 mg) and the adsorptive capacity is high. Thus only 0.06 g is required per dose and therefore, tea leaves are an excellent adsorbent for this drug. The present study leads to an important conclusion that tea leaves have the potential to be used as a safe and effective pharmaceutical adsorbent for the studied drugs.

REFERENCES

Anderson, R.A. and M.M. Polansky, 2002. Tea enhances insulin activity. J. Agric. Food Chem., 50: 7182-7186.

Davies, M.J., J.T. Judd, D.J. Baer, B.A. Clevidence, D.R. Paul, A.J. Edwards, S.A. Wiseman, R.A. Muesing and S.C. Chen, 2003. Black tea consumption reduces total and LDL cholesterol in mildly hypercholesterolemic adults. J. Nutr., 133: 3298S-3302S.

Florence, A.T. and D. Attwood, 1998. Physicochemical Principles of Pharmacy. Macmillan Press Ltd., London, pp: 218.

Hara, Y., 2001. Green Tea, Health Benefits and Applications. Dekker, New York.

Higdon, J.V. and B. Frei, 2003. Tea catechins and polyphenols: Health effects, metabolism and antioxidant functions. Crit. Rev. Food Sci. Nutr., 43: 89-143.

Ikeda, M., C. Suzuki, K. Umegaki, K. Saito, M. Tabuchi and T. Tomita, 2007. Preventive effects of green tea catechins on spontaneous stroke in rats. Med. Sci. Monit., 13: 40-45.

James, L.P. and G.L. Kearns, 1995. Cyclic antidepressant toxicity in children and adolescents. J. Clin. Pharmacol., 35: 343-350.

Mukhtar, H. and N. Ahmad, 2000. Tea polyphenols: Prevention of cancer and optimizing health. Am. J. Clin. Nutr., 71: 1698S-1702S.