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Studies of Partial Molar Volumes of Some Narcotic-Analgesic Drugs in Aqueous-Alcoholic Mixtures at 25°C

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Abstract Partial molar volumes of the drugs Parvon Spas, Parvon Forte, Tramacip, and Parvodex in aqueous mixtures of methanol (MeOH), ethanol (EtOH), and propan-1-ol (1-PrOH) have been determined. The data have been evaluated using the Masson equation. The parameters, apparent molar volumes (ϕ_v), partial molar volumes (ϕ_v^0), and S_v values (experimental slopes) have been interpreted in terms of solute–solvent interactions. In addition, these studies have also been extended to determine the effect of these drugs on the solvation behavior of an electrolyte (sodium chloride), a surfactant (sodium dodecyl sulfate), and a non-electrolyte (sucrose). It can be inferred from these studies that all drug cations can be regarded as structure makers/promoters due to hydrophobic hydration. Furthermore, the results are correlated to understand the solution behavior of drugs in aqueous-alcoholic systems, as a function of the nature of the alcohol and solutes.

Keywords Density · Drug · Ethanol · Methanol · 1-Propanol · Water

1 Introduction

Physicochemical properties of drugs are of great interest to understand 'drug action' at the molecular level. The pharmadynamics and pharmakinetics [1], i.e., what a drug does to the body and what the body does to the drug, must be regarded as the ultimate consequence of physicochemical interactions [2] between the drug and functionally important molecules in the living organism. Most drugs are organic molecules with both hydrophilic and hydrophobic groups due to which these molecules show specific as well as electrostatic interactions [3]. Thus, knowledge of the physicochemical

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properties of drugs plays an important role to understand their physiological actions which is highly dependent upon the solution behavior.

As a part of a long-term objective to investigate thermodynamic aspects of biochemical processes involving such drug-molecular interactions, we have carried out measurements of partial molar volumes of some narcotic-analgesic drugs which are centrally active analgesics that are effective for the management of moderate-to-moderately severe pain. These studies are carried out in aqueous mixtures of alcohols (methanol (MeOH), ethanol (EtOH), and propan-1-ol (1-PrOH)) which also includes the effect of these drugs on the solution behavior of sodium chloride (NaCl), sodium dodecyl sulfate (SDS), sucrose, etc.

2 Experimental

Drugs, namely, Parvon Spas (PS) containing paracetamol, dicyclomine hydrochloride, and dextropropoxyphene hydrochloride; Parvon Forte (PF) containing ibuprofen and dextropropoxyphene hydrochloride; Parvodex (PD) containing only dextropropoxyphene hydrochloride; and Tramacip (TM) containing only trammadol hydrochloride, are classified as narcotic-analgesic drugs. The drugs PS, PF, and PD were procured from Jagsonpal Pharmaceuticals Ltd., Faridabad, while Tramacip was obtained from CIPLA Ltd., Mumbai.

These drugs and solutes, viz. sodium chloride (99.9% purity, AR grade, S.D. Fine-Chem. Pvt. Ltd.), sodium dodecyl sulfate (extra pure, AR grade, SRL Pvt. Ltd. Mumbai), and sucrose (AR grade, LOBA Chemie, Mumbai) were used after drying them in a vacuum oven. MeOH (AR grade, S.D. Fine-Chem. Ltd.), EtOH (AR grade, Bengal Chemicals and Pharmaceuticals Ltd.), and 1-PrOH (AR grade, S.D. Fine-Chem. Ltd.) were dried on 4-Å molecular sieves for 24 h and were purified as reported in the literature [4,5]. Doubly distilled water was used in the entire work.

For measurements of the densities of the drugs, various alcohol + water mixtures were prepared by volume (V/V). All measurements were carried out at 25 ± 0.01°C in a water thermostat using a calibrated sealable pycnometer. The density values for MeOH, EtOH, and 1-PrOH were in good agreement with literature values [5,6].

3 Results and Discussion

Density, a physical property of solutions, offers useful information for evaluating partial molar volumes and apparent molar volumes of solutes in solvent systems, which in turn can explain solvent–solvent and drug/solute–solvent interactions [7,8].

The densities of various drug solutions have been measured in binary aqueous alcoholic mixtures containing 30, 50, 70, and 90% (V/V) alcohol at 25°C (Table 1). Similarly, densities of NaCl, SDS, and sucrose containing fixed amounts of drugs have also been measured in aqueous-alcoholic mixtures containing 40, 50, 60, and 70% (V/V) alcohol at 25°C and are reported in Tables 2–4.

From a look at Tables 1–4, it is observed that the density increases with an increase in the concentration of the drug. This may be attributed to the shrinkage in the volume, which in turn is due to the presence of solute/drug molecules [8]. In other words, the

Table 1 Molar concentration C(mol · dm^{-3}) and density ρ(g · cm^{-3}) for drugs PS, PF, PD, and TM in various aqueous-alcoholic mixtures

C	ρ											
	MeOH + H_2O				EtOH + H_2O				1-PrOH + H_2O			
	90%	70%	50%	30%	90%	70%	50%	30%	90%	70%	50%	30%
PS												
0.000	0.7981	0.8532	0.8896	0.9380	0.7861	0.8477	0.8856	0.9359	0.8213	0.8714	0.9061	0.9533
0.0384	0.7982	0.8533	0.8897	0.9381	0.7862	0.8478	0.8857	0.9360	0.8214	0.8715	0.9062	0.9534
0.0745	0.7983	0.8534	0.8898	0.9382	0.7863	0.8479	0.8858	0.9361	0.8215	0.8716	0.9063	0.9535
0.1082	0.7984	0.8535	0.8899	0.9383	0.7864	0.8480	0.8859	0.9362	0.8216	0.8717	0.9064	0.9536
0.1398	0.7985	0.8536	0.8900	0.9384	0.7865	0.8481	0.886	0.9363	0.8217	0.8718	0.9065	0.9537
0.1697	0.7986	0.8537	0.8901	0.9385	0.7866	0.8482	0.8861	0.9364	0.8218	0.8719	0.9066	0.9538
PF												
0.000	0.7981	0.8532	0.8896	0.9380	0.7861	0.8477	0.8856	0.9359	0.8213	0.8714	0.9061	0.9533
0.0292	0.7983	0.8534	0.8898	0.9382	0.7863	0.8479	0.8858	0.9361	0.8215	0.8716	0.9063	0.9535
0.0566	0.7985	0.8536	0.8900	0.9384	0.7865	0.8481	0.8860	0.9363	0.8217	0.8718	0.9065	0.9537
0.0823	0.7987	0.8538	0.8902	0.9386	0.7867	0.8483	0.8862	0.9365	0.8219	0.872	0.9067	0.9539
0.1069	0.7989	0.8540	0.8904	0.9388	0.7869	0.8485	0.8864	0.9367	0.8221	0.8722	0.9069	0.9541
0.1296	0.7991	0.8542	0.8906	0.939	0.7871	0.8487	0.8866	0.9369	0.8223	0.8724	0.9071	0.9543
PD												
0.000	0.7981	0.8532	0.8896	0.9380	0.7861	0.8477	0.8856	0.9359	0.8213	0.8714	0.9061	0.9533
0.0171	0.7986	0.8537	0.8900	0.9384	0.7866	0.8482	0.8861	0.9364	0.8217	0.8718	0.9065	0.9537
0.0331	0.7991	0.8543	0.8905	0.9389	0.7871	0.8487	0.8866	0.9369	0.8221	0.8722	0.9069	0.9541
0.0484	0.7996	0.8548	0.8910	0.9394	0.7876	0.8492	0.8871	0.9374	0.8225	0.8726	0.9073	0.9545
0.0625	0.8001	0.8553	0.8915	0.9399	0.7881	0.8497	0.8876	0.9379	0.8229	0.8730	0.9077	0.9549
0.0761	0.8006	0.8558	0.892	0.9404	0.7886	0.8502	0.8881	0.9384	0.8233	0.8734	0.9081	0.9553
TM												
0.000	0.7981	0.8532	0.8896	0.9380	0.7861	0.8477	0.8856	0.9359	0.8213	0.8714	0.9061	0.9533
0.0213	0.7984	0.8535	0.8900	0.9383	0.7864	0.848	0.8859	0.9362	0.8217	0.8718	0.9065	0.9537
0.0416	0.7987	0.8538	0.8904	0.9386	0.7867	0.8483	0.8862	0.9365	0.8221	0.8722	0.9069	0.9541
0.0605	0.7990	0.8541	0.8908	0.9389	0.7870	0.8486	0.8865	0.9368	0.8225	0.8726	0.9073	0.9545
0.0784	0.7993	0.8544	0.8912	0.9392	0.7873	0.8489	0.8868	0.9371	0.8229	0.8730	0.9077	0.9549
0.0954	0.7996	0.8547	0.8916	0.9395	0.7876	0.8492	0.8871	0.9374	0.8233	0.8734	0.9081	0.9553

Table 2 Molar concentration C (mol · dm^{-3}) and density ρ (g · cm^{-3}) for NaCl in presence of drugs PS, PF, PD, and TM in aqueous-alcoholic mixtures

C	ρ											
	MeOH + H_2O				EtOH + H_2O				1-PrOH + H_2O			
	70%	60%	50%	40%	70%	60%	50%	40%	70%	60%	50%	40%
PS												
0.000	0.9201	0.9390	0.9600	0.9809	0.9050	0.9283	0.9507	0.9750	0.948	0.9628	0.9827	1.0000
0.166	0.9202	0.9391	0.9601	0.9810	0.9051	0.9284	0.9508	0.9751	0.9481	0.9629	0.9828	1.0001
0.231	0.9203	0.9392	0.9602	0.9811	0.9052	0.9285	0.9509	0.9752	0.9482	0.9630	0.9829	1.0002
0.278	0.9204	0.9393	0.9603	0.9812	0.9053	0.9286	0.951	0.9753	0.9483	0.9631	0.9830	1.0003
0.317	0.9205	0.9394	0.9604	0.9813	0.9054	0.9287	0.9511	0.9754	0.9484	0.9632	0.9831	1.0004
0.349	0.9206	0.9395	0.9605	0.9814	0.9055	0.9288	0.9512	0.9755	0.9485	0.9633	0.9832	1.0005
PF												
0.000	0.9257	0.9421	0.9650	0.9880	0.9056	0.9297	0.9532	0.9768	0.9587	0.9676	0.9903	1.0130
0.166	0.9258	0.9422	0.9651	0.9881	0.9057	0.9298	0.9533	0.9769	0.9588	0.9677	0.9904	1.0131
0.231	0.9259	0.9423	0.9652	0.9882	0.9058	0.9299	0.9534	0.9770	0.9589	0.9678	0.9905	1.0132
0.278	0.9260	0.9424	0.9653	0.9883	0.9059	0.9300	0.9535	0.9771	0.959	0.9679	0.9906	1.0133
0.317	0.9261	0.9425	0.9654	0.9884	0.906	0.9301	0.9536	0.9772	0.9591	0.968	0.9907	1.0134
0.349	0.9262	0.9426	0.9655	0.9885	0.9061	0.9302	0.9537	0.9773	0.9592	0.9681	0.9908	1.0135
PD												
0.000	0.9412	0.9663	0.9910	1.0780	0.9318	0.9518	0.9819	1.066	0.9637	0.9943	1.0139	1.1050
0.166	0.9413	0.9664	0.9911	1.0781	0.9319	0.9519	0.982	1.0661	0.9638	0.9944	1.0140	1.1051
0.231	0.9414	0.9665	0.9912	1.0782	0.932	0.9520	0.9821	1.0662	0.9639	0.9945	1.0141	1.1052
0.278	0.9415	0.9666	0.9913	1.0783	0.9321	0.9521	0.9822	1.0663	0.9640	0.9946	1.0142	1.1053
0.317	0.9416	0.9667	0.9914	1.0784	0.9322	0.9522	0.9823	1.0664	0.9641	0.9947	1.0143	1.1054
0.349	0.9417	0.9668	0.9915	1.0785	0.9323	0.9523	0.9824	1.0665	0.9642	0.9948	1.0144	1.1055
TM												
0.000	0.9360	0.9575	0.9710	0.9991	0.9204	0.9403	0.9602	0.9902	0.9647	0.9881	0.9953	1.0219
0.166	0.9361	0.9576	0.9711	0.9992	0.9205	0.9404	0.9603	0.9903	0.9648	0.9882	0.9954	1.0220
0.231	0.9362	0.9577	0.9712	0.9993	0.9206	0.9405	0.9604	0.9904	0.9649	0.9883	0.9955	1.0221
0.278	0.9363	0.9578	0.9713	0.9994	0.9207	0.9406	0.9605	0.9905	0.965	0.9884	0.9956	1.0222
0.317	0.9364	0.9579	0.9714	0.9995	0.9208	0.9407	0.9606	0.9906	0.9651	0.9885	0.9957	1.0223
0.349	0.9365	0.958	0.9715	0.9996	0.9209	0.9408	0.9607	0.9907	0.9652	0.9886	0.9958	1.0224

Table 3 Molar concentration C(mol · dm^{-3}) and density ρ(g · cm^{-3}) for SDS in presence of drugs PS, PF, PD, and TM in aqueous-alcoholic mixtures

C	ρ											
	MeOH + H_2O				EtOH + H_2O				1-PrOH + H_2O			
	70%	60%	50%	40%	70%	60%	50%	40%	70%	60%	50%	40%
PS												
0.000	0.9201	0.9390	0.9600	0.9809	0.905	0.9283	0.9507	0.9750	0.9480	0.9628	0.9827	1.0000
0.047	0.9203	0.9392	0.9602	0.9811	0.9052	0.9285	0.9509	0.9752	0.9482	0.963	0.9829	1.0002
0.065	0.9205	0.9394	0.9604	0.9813	0.9054	0.9287	0.9511	0.9754	0.9484	0.9632	0.9831	1.0004
0.079	0.9207	0.9396	0.9606	0.9815	0.9056	0.9289	0.9513	0.9756	0.9486	0.9634	0.9833	1.0006
0.090	0.9209	0.9398	0.9608	0.9817	0.9058	0.9291	0.9515	0.9758	0.9488	0.9636	0.9835	1.0008
0.099	0.9211	0.9400	0.9610	0.9819	0.906	0.9293	0.9517	0.9760	0.9490	0.9638	0.9837	1.0010
PF												
0.000	0.9257	0.9421	0.9650	0.9880	0.9056	0.9297	0.9532	0.9768	0.9587	0.9676	0.9903	1.0130
0.047	0.9259	0.9423	0.9652	0.9882	0.9058	0.9299	0.9534	0.9770	0.9589	0.9678	0.9905	1.0132
0.065	0.9261	0.9425	0.9654	0.9884	0.906	0.9301	0.9536	0.9772	0.9591	0.968	0.9907	1.0134
0.079	0.9263	0.9427	0.9656	0.9886	0.9062	0.9303	0.9538	0.9774	0.9593	0.9682	0.9909	1.0136
0.090	0.9265	0.9429	0.9658	0.9888	0.9064	0.9305	0.954	0.9776	0.9595	0.9684	0.9911	1.0138
0.099	0.9267	0.9431	0.9660	0.9890	0.9066	0.9307	0.9542	0.9778	0.9597	0.9686	0.9913	1.0140
PD												
0.000	0.9412	0.9663	0.9910	1.078	0.9318	0.9518	0.9819	1.066	0.9637	0.9943	1.0139	1.1050
0.047	0.9414	0.9665	0.9912	1.0782	0.932	0.952	0.9821	1.0662	0.9639	0.9945	1.0141	1.1052
0.065	0.9416	0.9667	0.9914	1.0784	0.9322	0.9522	0.9823	1.0664	0.9641	0.9947	1.0143	1.1054
0.079	0.9418	0.9669	0.9916	1.0786	0.9324	0.9524	0.9825	1.0666	0.9643	0.9949	1.0145	1.1056
0.090	0.942	0.9671	0.9918	1.0788	0.9326	0.9526	0.9827	1.0668	0.9645	0.9951	1.0147	1.1058
0.099	0.9422	0.9673	0.9920	1.0790	0.9328	0.9528	0.9829	1.067	0.9647	0.9953	1.0149	1.106
TM												
0.000	0.9360	0.9575	0.9710	0.9991	0.9201	0.9403	0.9602	0.9902	0.9647	0.9881	0.9953	1.0219
0.047	0.9362	0.9577	0.9712	0.9993	0.9203	0.9405	0.9604	0.9904	0.9649	0.9883	0.9955	1.0221
0.065	0.9364	0.9579	0.9714	0.9995	0.9205	0.9407	0.9606	0.9906	0.9651	0.9885	0.9957	1.0223
0.079	0.9366	0.9581	0.9716	0.9997	0.9207	0.9409	0.9608	0.9908	0.9653	0.9887	0.9959	1.0225
0.090	0.9368	0.9583	0.9718	0.9999	0.9209	0.9411	0.9610	0.9910	0.9655	0.9889	0.9961	1.0227
0.099	0.9370	0.9585	0.9720	1.0000	0.9211	0.9413	0.9612	0.9912	0.9657	0.9891	0.9963	1.0229

Table 4 Molar concentration C (mol · dm^{-3}) and density ρ (g · cm^{-3}) for sucrose in presence of drugs PS, PF, PD, and TM in aqueous-alcoholic mixtures

C	ρ											
	MeOH + H_2O				EtOH + H_2O				1-PrOH + H_2O			
	70%	60%	50%	40%	70%	60%	50%	40%	70%	60%	50%	40%
PS												
0.000	0.9201	0.9390	0.9600	0.9809	0.9050	0.9283	0.9507	0.9750	0.948	0.9628	0.9827	1.0000
0.043	0.9203	0.9392	0.9602	0.9811	0.9052	0.9285	0.9509	0.9752	0.9482	0.963	0.9829	1.0002
0.060	0.9205	0.9394	0.9604	0.9813	0.9054	0.9287	0.9511	0.9754	0.9484	0.9632	0.9831	1.0004
0.072	0.9207	0.9396	0.9606	0.9815	0.9056	0.9289	0.9513	0.9756	0.9486	0.9634	0.9833	1.0006
0.082	0.9209	0.9398	0.9608	0.9817	0.9058	0.9291	0.9515	0.9758	0.9488	0.9636	0.9835	1.0008
0.091	0.9211	0.9400	0.9610	0.9819	0.9060	0.9293	0.9517	0.9760	0.949	0.9638	0.9837	1.0010
PF												
0.000	0.9257	0.9421	0.9650	0.9880	0.9056	0.9297	0.9532	0.9768	0.9587	0.9676	0.9903	1.013
0.043	0.9259	0.9423	0.9652	0.9882	0.9058	0.9299	0.9534	0.9770	0.9589	0.9678	0.9905	1.0132
0.060	0.9261	0.9425	0.9654	0.9884	0.906	0.9301	0.9536	0.9772	0.9591	0.968	0.9907	1.0134
0.072	0.9263	0.9427	0.9656	0.9886	0.9062	0.9303	0.9538	0.9774	0.9593	0.9682	0.9909	1.0136
0.082	0.9265	0.9429	0.9658	0.9888	0.9064	0.9305	0.954	0.9776	0.9595	0.9684	0.9911	1.0138
0.091	0.9267	0.9431	0.9660	0.9890	0.9066	0.9307	0.9542	0.9778	0.9597	0.9686	0.9913	1.0140
TM												
0.000	0.9412	0.9663	0.9910	1.0780	0.9318	0.9518	0.9819	1.0660	0.9637	0.9943	1.0139	1.105
0.043	0.9414	0.9665	0.9912	1.0782	0.932	0.952	0.9821	1.0662	0.9639	0.9945	1.0141	1.1052
0.060	0.9416	0.9667	0.9914	1.0784	0.9322	0.9522	0.9823	1.0664	0.9641	0.9947	1.0143	1.1054
0.072	0.9418	0.9669	0.9916	1.0786	0.9324	0.9524	0.9825	1.0666	0.9643	0.9949	1.0145	1.1056
0.082	0.9420	0.9671	0.9918	1.0788	0.9326	0.9526	0.9827	1.0668	0.9645	0.9951	1.0147	1.1058
0.091	0.9422	0.9673	0.9920	1.0790	0.9328	0.9528	0.9829	1.0670	0.9647	0.9953	1.0149	1.106
PD												
0.000	0.9360	0.9575	0.9710	0.9991	0.9201	0.9403	0.9602	0.9902	0.9647	0.9881	0.9953	1.0219
0.043	0.9362	0.9577	0.9712	0.9993	0.9203	0.9405	0.9604	0.9904	0.9649	0.9883	0.9955	1.0221
0.060	0.9364	0.9579	0.9714	0.9995	0.9205	0.9407	0.9606	0.9906	0.9651	0.9885	0.9957	1.0223
0.072	0.9366	0.9581	0.9716	0.9997	0.9207	0.9409	0.9608	0.9908	0.9653	0.9887	0.9959	1.0225
0.082	0.9368	0.9583	0.9718	0.9999	0.9209	0.9411	0.961	0.9910	0.9655	0.9889	0.9961	1.0227
0.091	0.9370	0.9585	0.9720	1.0000	0.9211	0.9413	0.9612	0.9912	0.9657	0.9891	0.9963	1.0229

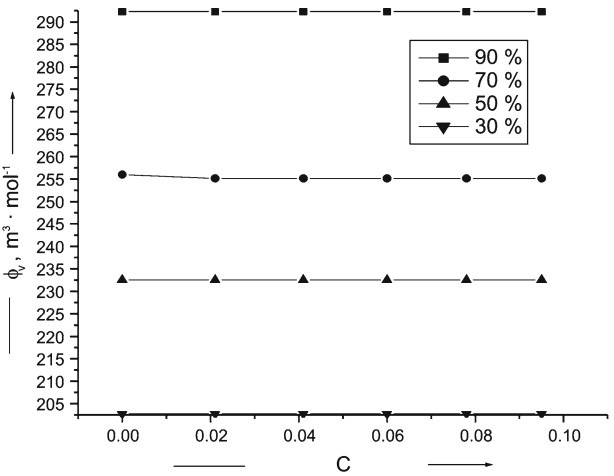

Fig. 1 Plot of apparent molar volumes (ϕ_v) versus concentration of drug PD in aqueous mixtures of 1-PrOH

increase in density may be interpreted due to the enhanced structure of the solvent mixture due to the added drug for different alcoholic systems; the density values vary as

$$1\text{-PrOH} + H_2O > MeOH + H_2O > EtOH + H_2O$$

which is consistent with the density of different alcohols [5,6].

From the accurate density values, apparent molar volumes (ϕ_v) have been calculated using the equation,

$$\phi_v = M/\rho + (\rho_0 - \rho)1000/C\rho_0 \tag{1}$$

where ρ and ρ_0 are the densities of the solution and solvent, respectively. M is the molar mass of the drugs and C is the molar concentration.

It is found that, in each case, ϕ_v values are found to be strikingly independent of drug concentration (Fig. 1). However, the ϕ_v values of the drugs in aqueous mixtures of alcohols decrease in the order,

$$\text{Water–MeOH} \approx \text{Water–EtOH} > \text{Water–1-PrOH}$$

This sequence appears to suggest that the hydrophobic chain of the alcohol is the cause of the observed order in ϕ_v values. The change in this property in aqueous mixtures of alcohols should therefore reflect the changes occurring in the environment of the drug. These observations, therefore, strongly suggest that considerably more structure should be disrupted in aqueous mixtures of 1-PrOH.

Also, drug and alcohol molecules are characterized by the presence of hydrophobic and hydrophilic centers leading to two different types of hydration [9]. Both compete for water structure organization [10]. The addition of drug molecules to water causes

the rupture of the tetrahedral structure of water. When two nonpolar regions come closer together, these regions are shielded to a greater extent from interactions with water molecules leading to the collapse of the quasi-crystalline structure of water [11]. The nature of hydrophobic interactions of drug molecules with water changes to a different extent with the addition of a different alcohol.

Since the nature of the interacting groups is different, the changes in thermodynamic properties are expected. The changes can be attributed to specific solvation effects and hydrophobic effects that act in opposite directions. Specific solvation effects are dependent mainly on the composition of the solvent mixture, being greatest for strongly solvated drugs. The hydrophobic effect, on the other hand, increases with the size of solute–solvent molecules [8].

It has been cited in the literature [8] that drug molecules behave in a manner similar to tetraalkylammonium salts in aqueous-alcoholic systems where the concentration dependence of ϕ_v values of these drugs has been interpreted in terms of the true volume of the solute and solvent and the loss of free volume near the solute during hydrophobic hydration [12].

Further evidence of this effect is obtained when ϕ_v data are analyzed in terms of the partial molar volume of the drugs using the Masson equation [13],

$$\phi_v = \phi_v^0 + S_v C^{1/2} \tag{2}$$

where S_v is the experimental slope which depends on the charge and nature/type of the solute, and the partial molar volume (ϕ_v^0) is the intercept that measures the solute–solvent interactions. These values are obtained from a least-squares fit. S_v values are found to be negative, indicating weak ion–ion interactions. A possible explanation for the presence of negative S_v values, i.e., negative slopes, is that at infinite dilution, drugs are completely dissociated in all these solvent mixtures which is different from the situation at higher concentrations of drugs. Therefore, an appreciable inter-ionic penetration occurs and gives rise to negative slopes which leads to weak ion–ion interactions and strong ion–solvent interactions. These negative values of S_v for different compositions also suggest the presence of cation–anion penetration [14,15], and this happens due to the competition between the drug ions to occupy the void space of the large solvent molecules. Also, it is seen (Tables 5–8) that there is no appreciable variation in S_v with a change in composition of a particular aqueous-alcoholic system, even when the alcohol component changes from MeOH to 1-PrOH. Furthermore, it has also been observed that these values are independent of the nature of the drug. Similar observations have been reported by Parmar et al. [14] for ammonium, sodium, and potassium phosphates in binary aqueous solutions of urea, and for citric acid and tartaric acid [15] in water and binary aqueous mixtures of EtOH at various temperatures in which S_v values are reported to be negative. Also, for a number of hydrochloride-type drugs, either negative or very small values of S_v have been reported in the literature [16], indicating weak ion–ion interactions.

ϕ_v^0 values of the drugs are found to be positive and quite large in aqueous mixtures of alcohols and have been summarized in Table 5. The data suggest that the magnitude

Table 5 $\phi_v^0(m^3 \cdot mol^{-1})$ and $S_v(m^3 \cdot kg^{1/2} \cdot mol^{-3/2})$ values of the drugs Parvon Spas (PS), Parvon Forte (PF), Parvodex (PD), and Tramacip (TM) in aqueous mixtures of alcohols at 25°C

	30		50		70		90	
	ϕ_v^0	S_v	ϕ_v^0	S_v	ϕ_v^0	S_v	ϕ_v^0	S_v
Drug/MeOH ↓ (V/V%)→								
PS	178.6	−0.81	188.3	−0.97	196.4	−0.87	205.9	−0.81
PF	234.5	−1.00	247.3	−0.99	257.8	−0.86	264.9	−1.00
TM	319.7	−0.98	337.1	−0.90	351.5	−0.90	358.9	−0.98
PD	400.3	−0.99	422.0	−0.91	440.1	−0.91	463.0	−0.99
Drug/EtOH ↓ (V/V%)→								
PS	179.1	−0.95	189.3	−0.97	197.8	−0.98	209.1	−0.81
PF	235.0	−0.93	248.4	−0.99	259.5	−0.99	268.7	−1.00
TM	320.4	−0.90	338.6	−0.90	353.7	−0.96	363.5	−0.98
PD	401.2	−0.91	424.0	−0.91	442.9	−0.95	459.3	−0.99
Drug/1-PrOH ↓ (V/V%)→								
PS	175.9	−0.93	185.0	−0.81	192.4	−0.98	200.3	−0.93
PF	230.7	−0.94	242.7	−1.00	252.4	−1.00	257.7	−0.94
TM	314.5	−0.92	330.9	−0.98	344.1	−0.98	357.3	−0.92
PD	393.8	−0.91	414.4	−0.99	430.9	−0.99	442.6	−0.90

Table 6 $\phi_v^0(m^3 \cdot mol^{-1})$ and $S_v(m^3 \cdot kg^{1/2} \cdot mol^{-3/2})$ values of NaCl in presence of drugs Parvon Spas (PS), Parvon Forte (PF), Parvodex (PD), and Tramacip (TM) in aqueous mixtures of alcohols at 25°C

	40		50		60		70	
	ϕ_v^0	S_v	ϕ_v^0	S_v	ϕ_v^0	S_v	ϕ_v^0	S_v
Drug/MeOH ↓ (V/V%)→								
PS	55.06	−0.98	56.30	−0.81	57.60	−0.98	58.97	−0.93
PF	54.39	−0.90	55.90	−0.94	57.00	−1.00	58.00	−0.94
TM	53.55	−0.98	55.30	−0.98	56.30	−0.98	57.82	−0.98
PD	48.87	−0.99	50.10	−0.99	54.60	−0.99	56.32	−0.99
Drug/EtOH ↓ (V/V%)→								
PS	55.12	−0.81	56.78	−0.98	58.37	−0.98	60.11	−0.81
PF	55.00	−1.00	56.60	−1.00	58.27	−1.00	60.07	−1.00
TM	54.12	−0.98	56.12	−0.98	57.51	−0.98	58.95	−0.98
PD	52.54	−0.99	54.66	−0.99	56.70	−0.99	58.12	−0.99
Drug/1-PrOH ↓ (V/V%)→								
PS	53.50	−0.98	54.62	−0.96	55.94	−0.97	56.96	−0.98
PF	52.68	−1.00	54.10	−0.95	55.62	−1.00	56.22	−1.00
TM	51.13	−0.98	52.94	−0.98	54.26	−0.98	55.91	−0.98
PD	50.41	−0.99	52.63	−0.99	53.86	−0.99	55.88	−0.99

of ϕ_v^0 values of the drugs follows the sequence (Fig. 2),

$$PD > TM > PF > PS$$

which indicates solute–solvent interactions are maximum for PD and least for PS.

As is clear from the molecular structure of drugs, PD contains dextropropoxyphene hydrochloride, TM has only tramadol hydrochloride, PS does contain paracetamol and dicyclomine hydrochloride in addition to dextropropoxyphene hydrochloride, whereas

Table 7 $\phi_v^0(m^3 \cdot mol^{-1})$ and $S_v(m^3 \cdot kg^{1/2} \cdot mol^{-3/2})$ values of SDS in presence of drugs Parvon Spas (PS), Parvon Forte (PF), Parvodex (PD), and Tramacip (TM) in aqueous mixtures of alcohols at 25°C

	40		50		60		70	
	ϕ_v^0	S_v	ϕ_v^0	S_v	ϕ_v^0	S_v	ϕ_v^0	S_v
Drug/MeOH ↓ (V/V%)→								
PS	195.8	−0.98	204.3	−0.81	213.1	−0.98	221.3	−0.97
PF	193.0	−1.00	202.2	−1.00	211.8	−1.00	218.8	−1.00
TM	188.6	−0.98	199.8	−0.98	205.3	−0.98	214.4	−0.98
PD	159.6	−0.99	191.8	−0.99	201.7	−0.99	212.1	−0.99
Drug/EtOH↓ (V/V%)→								
PS	198.1	−0.96	208.1	−0.81	217.7	−0.96	228.0	−0.96
PF	197.4	−0.95	207.1	−1.00	217.1	−0.95	227.7	−0.95
TM	192.1	−0.98	204.2	−0.98	212.5	−0.98	221.3	−0.98
PD	163.8	−0.99	195.4	−0.99	207.7	−0.99	216.2	−0.99
Drug/1-PrOH ↓ (V/V%)→								
PS	188.0	−0.96	195.4	−0.96	203.0	−0.83	209.0	−0.96
PF	183.3	−0.95	192.8	−0.95	201.8	−1.00	204.5	−0.95
TM	179.9	−0.98	190.0	−0.98	192.4	−0.98	202.6	−0.98
PD	150.4	−0.99	182.9	−0.99	190.8	−0.99	200.1	−0.99

Table 8 $\phi_v^0(m^3 \cdot mol^{-1})$ and $S_v(m^3 \cdot kg^{1/2} \cdot mol^{-3/2})$ values of sucrose in presence of drugs Parvon Spas (PS), Parvon Forte (PF), Parvodex (PD), and Tramacip (TM) in aqueous mixtures of alcohols at 25°C

	40		50		60		70	
	ϕ_v^0	S_v	ϕ_v^0	S_v	ϕ_v^0	S_v	ϕ_v^0	S_v
Drug/MeOH ↓ (V/V%)→								
PS	250.4	−0.93	260.0	−0.93	270.2	−0.93	279.8	−0.98
PF	247.3	−1.00	257.1	−1.00	268.4	−1.00	276.7	−0.94
TM	240.3	−0.98	255.9	−0.98	261.8	−0.98	271.8	−0.98
PD	229.5	−0.99	246.2	−0.99	257.3	−0.99	264.6	−0.99
Drug/EtOH ↓ (V/V%)→								
PS	253.2	−0.98	264.1	−0.93	275.1	−0.81	287.8	−0.98
PF	252.3	−0.94	263.1	−1.00	274.6	−1.00	287.6	−0.94
TM	246.4	−0.98	260.4	−0.98	269.8	−0.98	279.0	−0.98
PD	234.2	−0.99	250.6	−0.99	264.5	−0.99	273.4	−0.99
Drug/1-PrOH ↓ (V/V%)→								
PS	239.0	−0.81	248.9	−0.96	257.5	−0.96	260.5	−0.93
PF	236.4	−1.00	246.0	−0.95	255.3	−0.95	260.0	−1.00
TM	232.3	−0.98	244.3	−0.98	247.6	−0.98	258.8	−0.98
PD	229.2	−0.99	235.5	−0.99	244.6	−0.99	256.9	−0.99

PF contains ibuprofen in addition to dextropropoxyphene hydrochloride. From these structures, it is evident that the contribution to ϕ_v^0 values is relatively large due to the hydrochloride moiety. Since PD and TM contain only a hydrochloride part, they contribute the maximum to ϕ_v^0, but in the case of PF, one component does not seem to participate, whereas in PS these values are inhibited to a certain extent because inter-component interactions of the amide group with the cations of other components are also not ruled out, thus offering the smallest values.

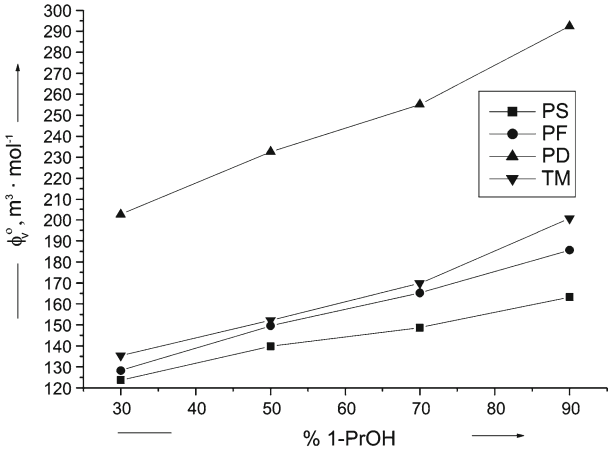

Fig. 2 Plot of partial molar volumes (ϕ_v^0) versus composition of 1-PrOH for drugs PS, PF, PD, and TM

The decrease in ϕ_v^0 values of the drugs with solvent composition is as follows:

$$\text{Water–MeOH} \approx \text{Water–EtOH} > \text{Water–1-PrOH}$$

This substantial decrease with an increase in alcoholic content in their respective aqueous mixtures seems to manifest the peculiar characteristics of the drugs and also supports the importance of the hydrophobic part of the alcohol as suggested earlier.

Out of the three alcohols, MeOH is the most capable of participating in hydrogen-bond formation [17] with water, appearing to induce solvophobic solvation of drugs, as it is well known that the addition of MeOH strengthens the water structure.

We now turn to the analysis of ϕ_v^0 data for NaCl, SDS, and sucrose in aqueous-alcoholic solutions of drugs. These data have been obtained using Masson's equation (2) and are reported in Tables 6–8.

The results show that ϕ_v^0 values of NaCl are practically independent of the nature of the drug as well as the nature of the solvent system. However, the ϕ_v^0 values of SDS and sucrose in solutions of drugs increase (Fig. 3) in the order,

$$\text{PD} < \text{TM} < \text{PF} < \text{PS}$$

Also, the effect of alcohol is found to decrease this parameter for SDS and sucrose (Fig. 4) in the order,

$$\text{Water–MeOH} \approx \text{Water–EtOH} > \text{Water–1-PrOH}$$

These orders are in agreement with the changes observed in the B-values [18] of these species in the presence of drugs. This large difference between the solution behavior of SDS and sucrose, together with the lack of differentiation with respect to NaCl, provides the clue to the probable hydrophobic interactions of the structural effect of the solvent system.

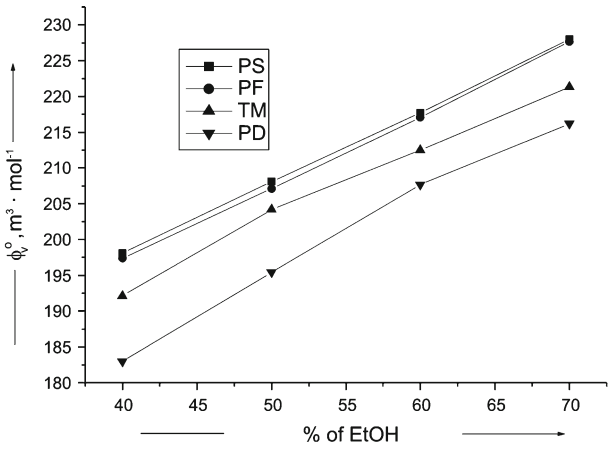

Fig. 3 Plot of partial molar volumes (ϕ_v^0) versus composition of EtOH for SDS in presence of drugs PS, PF, TM, and PD

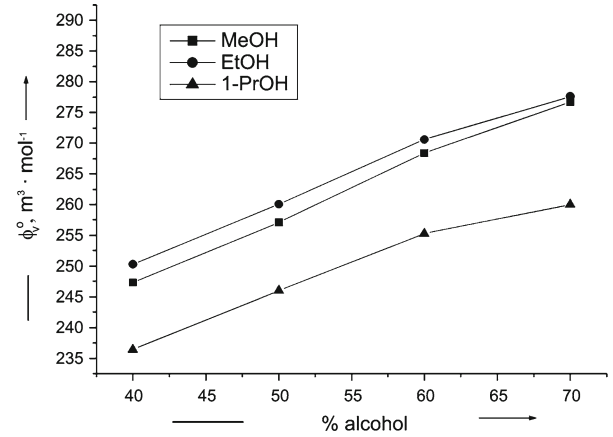

Fig. 4 Plot of apparent molar volumes (ϕ_v^0) versus composition of alcohol (MeOH, EtOH, and 1-PrOH) for sucrose in presence of drug PF

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