

Additional Sodium Chloride Equivalents and Freezing Point Depressions for Various Medicinal Solutions

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The NaCl equivalents, freezing point depressions of their aqueous solutions, and isotonic concentrations were determined for 78 different medicinal substances by using the cryoscopic method. The data are presented in a table to supplement those data for 332 different substances published previously.

IN 1958, HAMMARLUND and Pedersen-Bjergaard (1) presented a revised table of NaCl equivalents for 332 different medicinal substances used in the preparation of isotonic solutions. The values were all experimentally determined and included most of those substances readily available at that time and used in aqueous medicinal solutions.

The objective of this present investigation was to study in a similar manner 78 additional substances not included in the earlier study and to present the data in a suitable table to supplement the previously published data (1).

EXPERIMENTAL METHODS AND RESULTS

The method used for the measurement of the freezing points of the solutions was the same as that reported previously in detail (1). The freezing point depression measurements were made directly on various concentrations of the aqueous solutions of the experimental compounds by means of a Beckman differential thermometer. The freezing point measurements were corrected for the amount of disengaged ice, and -0.52° was used as the comparative freezing point for aqueous 0.9% NaCl solution which is isotonic with blood and tears. The substances tested were of U.S.P. or N.F. grade of purity or better. For those nonofficial substances, the grade of purity of each complied with the manufacturer's specifications. The NaCl equivalents and isotonic concentrations are reported to the nearest 0.01.

Table I lists the NaCl equivalents at various concentrations for all of the newly studied substances. To use these data, one should employ the NaCl

equivalent which represents the concentration nearest to the desired concentration of medicinal substance used.

Since some reference books, such as "The Merck Index" (2), have included the individual freezing point depressions, calculated from the previously published table of NaCl equivalents (1), these freezing point depression data are likewise included in Table I in addition to the NaCl equivalents and isotonic concentrations. Where practical, the NaCl equivalents and the corresponding freezing points are presented for six different concentrations instead of only four concentrations, as in the previous report (1).

Moreover, due to the relatively smaller number of substances in this current study, all data are listed in the single table, regardless of whether the drugs are usually available in pure form. Because of the recent interest in the colligative properties of their solutions, the freezing points and NaCl equivalents are included for some preparations, *i.e.*, phenothiazine derivatives, which are at present only used orally and not as isotonic solutions.

The term "isotonic solution" is used in its customary sense in this report—meaning that it freezes at the same temperature as normal saline solution, blood, and tears. Actually the term "isosmotic" is more correct since there are a number of isosmotic solutions which are not isotonic to human erythrocytes (3, 4). A term such as "isocolligative" or "isocryoscopic" might be even more descriptive in those cases where only a colligative property was investigated; such a term would not imply that a particular physiological membrane was employed as a reference.

SUMMARY

A supplemental table of NaCl equivalents and freezing point depressions at various concentrations for 78 different medicinal substances in aqueous solution is presented. Also given in the table is the percentage concentration (w/v) of the solute which, when used alone, will produce an aqueous solution that is isotonic with blood and tears.

REFERENCES

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TABLE I.—SODIUM CHLORIDE EQUIVALENTS AND FREEZING POINT DEPRESSIONS, °C.

Chemical	Concn. of Soln., NaCl Equivalents					At Isotonicity
	0.5%	1%	2%	3%	5%	
Adenosine-5-monophosphate	0.50 ^a 0.140 ^{ob}	0.41 ^a 0.234 ^{ob}
Aminocaproic acid	0.26 0.075°	0.26 0.148°	0.26 0.297°	0.26 0.444°	...	0.26 (3.52) ^c 0.52 (3.52) ^c
Amitriptyline HCl	0.24 0.070°	0.18 0.100°	0.11 0.125°	0.08 0.147°	0.06 0.177°	...
Ammonium carbonate	0.70	0.70	0.70 (1.29)
N.F. ^d	0.202°	0.405°	0.52° (1.29)
Ammonium lactate	0.33 0.093°	0.33 0.185°	0.33 0.370°	0.33 (2.76) 0.52° (2.76)

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Chemical	Concn. of Soln., NaCl Equivalents					At Isotonicity	
	0.5%	1%	2%	3%	5%		
Ammonium nitrate	0.69 <i>0.200°</i>	0.69 <i>0.400°</i>	0.69 <i>0.52°</i>	(1.30) (1.30)
Ammonium phosphate, dibasic	0.58 <i>0.165°</i>	0.55 <i>0.315°</i>	0.51 <i>0.52°</i>	(1.76) (1.76)
Ammonium sulfate	0.55 <i>0.158°</i>	0.55 <i>0.315°</i>	0.54 <i>0.52°</i>	(1.68) (1.68)
Benztropine mesylate N.F.	0.26 <i>0.073°</i>	0.21 <i>0.115°</i>	0.15 <i>0.170°</i>	0.12 <i>0.203°</i>	0.09 <i>0.242°</i>
Bethanechol chloride U.S.P. ⁴	0.50 <i>0.140°</i>	0.39 <i>0.225°</i>	0.32 <i>0.368°</i>	0.30 <i>0.512°</i>	...	0.30 <i>0.52°</i>	(3.05) (3.05)
Brompheniramine maleate N.F.	0.10 <i>0.026°</i>	0.09 <i>0.050°</i>	0.08 <i>0.084°</i>
Calcium disodium edetate U.S.P.	0.21 <i>0.061°</i>	0.21 <i>0.120°</i>	0.21 <i>0.240°</i>	0.20 <i>0.357°</i>	...	0.20 <i>0.52°</i>	(4.50) (4.50)
Chloramphenicol sodium succinate U.S.P.	0.14 <i>0.038°</i>	0.14 <i>0.078°</i>	0.14 <i>0.154°</i>	0.13 <i>0.230°</i>	0.13 <i>0.382°</i>	0.13 <i>0.52°</i>	(6.83) (6.83)
Chlordiazepoxide HCl N.F.	0.24 <i>0.068°</i>	0.22 <i>0.125°</i>	0.19 <i>0.220°</i>	0.18 <i>0.315°</i>	0.17 <i>0.487°</i>	0.16 <i>0.52°</i>	(5.50) (5.50)
Chloroquine sulfate	0.10 <i>0.028°</i>	0.09 <i>0.050°</i>	0.08 <i>0.090°</i>	0.07 <i>0.127°</i>	0.07 <i>0.195°</i>
Chlorpheniramine maleate U.S.P.	0.17 <i>0.048°</i>	0.15 <i>0.085°</i>	0.14 <i>0.165°</i>	0.13 <i>0.220°</i>	0.09 <i>0.265°</i>
Cyclizine HCl U.S.P.	0.20 <i>0.060°</i>
Cyclophosphamide N.F.	0.10 <i>0.031°</i>	0.10 <i>0.061°</i>	0.10 <i>0.125°</i>
Demecarium bromide	0.14 <i>0.038°</i>	0.12 <i>0.069°</i>	0.10 <i>0.108°</i>	0.08 <i>0.139°</i>	0.07 <i>0.192°</i>
Dexamethasone sodium phosphate N.F.	0.18 <i>0.050°</i>	0.17 <i>0.095°</i>	0.16 <i>0.180°</i>	0.15 <i>0.260°</i>	0.14 <i>0.410°</i>	0.13 <i>0.52°</i>	(6.75) (6.75)
Dextroamphetamine HCl	0.34 <i>0.097°</i>	0.34 <i>0.196°</i>	0.34 <i>0.392°</i>	0.34 <i>0.52°</i>	(2.64) (2.64)
Dextroamphetamine sul- fate U.S.P.	0.24 <i>0.069°</i>	0.23 <i>0.134°</i>	0.22 <i>0.259°</i>	0.22 <i>0.380°</i>	...	0.22 <i>0.52°</i>	(4.16) (4.16)
Dyclonine HCl	0.26 <i>0.073°</i>	0.24 <i>0.135°</i>	0.17 <i>0.190°</i>
Dimethylpyrindene maleate	0.13 <i>0.039°</i>	0.12 <i>0.070°</i>	0.11 <i>0.120°</i>
Diperodon HCl	0.15 <i>0.045°</i>	0.14 <i>0.079°</i>	0.13 <i>0.141°</i>
Edathamil disodium	0.24 <i>0.070°</i>	0.23 <i>0.132°</i>	0.22 <i>0.248°</i>	0.21 <i>0.360°</i>	...	0.20 <i>0.52°</i>	(4.44) (4.44)
Erythromycin lactobionate	0.08 <i>0.020°</i>	0.07 <i>0.040°</i>	0.07 <i>0.078°</i>	0.07 <i>0.115°</i>	0.06 <i>0.187°</i>
Furtrethonium iodide	0.24 <i>0.070°</i>	0.24 <i>0.133°</i>	0.22 <i>0.250°</i>	0.21 <i>0.360°</i>	...	0.20 <i>0.52°</i>	(4.44) (4.44)
Hexafluorenum bromide	0.12 <i>0.033°</i>	0.11 <i>0.065°</i>
Hexamethonium tartrate	0.16 <i>0.045°</i>	0.16 <i>0.089°</i>	0.16 <i>0.181°</i>	0.16 <i>0.271°</i>	0.16 <i>0.456°</i>	0.16 <i>0.52°</i>	(5.68) (5.68)
Histamine DiHCl	0.40 <i>0.115°</i>	0.40 <i>0.233°</i>	0.40 <i>0.466°</i>	0.40 <i>0.52°</i>	(2.24) (2.24)
Hyaluronidase N.F.	0.01 <i>0.004°</i>	0.01 <i>0.007°</i>	0.01 <i>0.013°</i>	0.01 <i>0.020°</i>	0.01 <i>0.033°</i>
Hydroxystilbamidine isethionate U.S.P.	0.20 <i>0.060°</i>	0.16 <i>0.090°</i>	0.12 <i>0.137°</i>	0.10 <i>0.170°</i>	0.07 <i>0.216°</i>
Imipramine HCl N.F.	0.20 <i>0.058°</i>	0.20 <i>0.110°</i>	0.13 <i>0.143°</i>
Kanamycin sulfate U.S.P.	0.08 <i>0.021°</i>	0.07 <i>0.041°</i>	0.07 <i>0.083°</i>	0.07 <i>0.125°</i>	0.07 <i>0.210°</i>
Maphenide HCl	0.27 <i>0.075°</i>	0.27 <i>0.153°</i>	0.27 <i>0.303°</i>	0.26 <i>0.448°</i>	...	0.25 <i>0.52°</i>	(3.55) (3.55)
Mepivacaine HCl N.F.	0.21 <i>0.060°</i>	0.21 <i>0.116°</i>	0.20 <i>0.230°</i>	0.20 <i>0.342°</i>	...	0.20 <i>0.52°</i>	(4.60) (4.60)
Metaraminol bitartrate U.S.P.	0.20 <i>0.060°</i>	0.20 <i>0.112°</i>	0.19 <i>0.210°</i>	0.18 <i>0.308°</i>	0.17 <i>0.505°</i>	0.17 <i>0.52°</i>	(5.17) (5.17)
Methdilazine HCl	0.12 <i>0.035°</i>	0.10 <i>0.056°</i>	0.08 <i>0.080°</i>	0.06 <i>0.093°</i>	0.04 <i>0.112°</i>
Methitural sodium	0.26 <i>0.074°</i>	0.25 <i>0.142°</i>	0.24 <i>0.275°</i>	0.23 <i>0.407°</i>	...	0.23 <i>0.52°</i>	(3.85) (3.85)
Methoxyphenamine HCl	0.26 <i>0.075°</i>	0.26 <i>0.150°</i>	0.26 <i>0.300°</i>	0.26 <i>0.450°</i>	...	0.26 <i>0.52°</i>	(3.47) (3.47)
p-Methylaminoethanol- phenol tartrate	0.18 <i>0.048°</i>	0.17 <i>0.095°</i>	0.16 <i>0.190°</i>	0.16 <i>0.282°</i>	0.16 <i>0.453°</i>	0.16 <i>0.52°</i>	(5.83) (5.83)
Methylodopate HCl	0.21 <i>0.063°</i>	0.21 <i>0.122°</i>	0.21 <i>0.244°</i>	0.21 <i>0.365°</i>	...	0.21 <i>0.52°</i>	(4.28) (4.28)

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Chemical	Concn. of Soln., NaCl Equivalents					At Isotonicity	
	0.5%	1%	2%	3%	5%		
<i>N</i> -Methylglucamine	0.20 <i>0.057°</i>	0.20 <i>0.111°</i>	0.18 <i>0.214°</i>	0.18 <i>0.315°</i>	0.18 <i>0.517°</i>	0.18 <i>0.52°</i>	(5.02) <i>(5.02)</i>
Methylphenidate HCl N.F.	0.22 <i>0.065°</i>	0.22 <i>0.127°</i>	0.22 <i>0.258°</i>	0.22 <i>0.388°</i>	...	0.22 <i>0.52°</i>	(4.07) <i>(4.07)</i>
Nalorphine HCl U.S.P.	0.24 <i>0.070°</i>	0.21 <i>0.121°</i>	0.18 <i>0.210°</i>	0.17 <i>0.288°</i>	0.15 <i>0.434°</i>	0.14 <i>0.52°</i>	(6.36) <i>(6.36)</i>
Oxyquinoline sulfate	0.24 <i>0.068°</i>	0.21 <i>0.113°</i>	0.16 <i>0.182°</i>	0.14 <i>0.236°</i>	0.11 <i>0.315°</i>
<i>d</i> -Pantothenyl alcohol	0.20 <i>0.053°</i>	0.18 <i>0.100°</i>	0.17 <i>0.193°</i>	0.17 <i>0.283°</i>	0.16 <i>0.468°</i>	0.16 <i>0.52°</i>	(5.60) <i>(5.60)</i>
Pargyline HCl	0.30 <i>0.083°</i>	0.29 <i>0.165°</i>	0.29 <i>0.327°</i>	0.28 <i>0.491°</i>	...	0.28 <i>0.52°</i>	(3.18) <i>(3.18)</i>
Phentolamine mesylate U.S.P.	0.18 <i>0.052°</i>	0.17 <i>0.096°</i>	0.16 <i>0.173°</i>	0.14 <i>0.244°</i>	0.13 <i>0.364°</i>	0.11 <i>0.52°</i>	(8.23) <i>(8.23)</i>
Polysorbate 80 U.S.P.	0.02 <i>0.005°</i>	0.02 <i>0.010°</i>	0.02 <i>0.020°</i>	0.02 <i>0.032°</i>	0.02 <i>0.055°</i>
Potassium acetate N.F.	0.59 <i>0.172°</i>	0.59 <i>0.342°</i>	0.59 <i>0.52°</i>	(1.53) <i>(1.53)</i>
Pralidoxime chloride	0.32 <i>0.092°</i>	0.32 <i>0.183°</i>	0.32 <i>0.364°</i>	0.32 <i>0.52°</i>	(2.87) <i>(2.87)</i>
Prochlorperazine edisylate U.S.P.	0.08 <i>0.020°</i>	0.06 <i>0.033°</i>	0.05 <i>0.048°</i>	0.03 <i>0.056°</i>	0.02 <i>0.065°</i>
Promazine HCl N.F.	0.18 <i>0.050°</i>	0.13 <i>0.077°</i>	0.09 <i>0.102°</i>	0.07 <i>0.112°</i>	0.05 <i>0.137°</i>
Propiomazine HCl	0.18 <i>0.050°</i>	0.15 <i>0.084°</i>	0.12 <i>0.133°</i>	0.10 <i>0.165°</i>	0.08 <i>0.215°</i>
Pyrithiazine HCl	0.22 <i>0.065°</i>	0.17 <i>0.095°</i>	0.11 <i>0.123°</i>	0.08 <i>0.140°</i>	0.06 <i>0.170°</i>
Sodium acetazolamide U.S.P.	0.24 <i>0.068°</i>	0.23 <i>0.135°</i>	0.23 <i>0.271°</i>	0.23 <i>0.406°</i>	...	0.23 <i>0.52°</i>	(3.85) <i>(3.85)</i>
Sodium bismuth thio- glycollate	0.20 <i>0.055°</i>	0.19 <i>0.107°</i>	0.18 <i>0.208°</i>	0.18 <i>0.303°</i>	0.17 <i>0.493°</i>
Sodium colistimethate U.S.P.	0.16 <i>0.045°</i>	0.15 <i>0.087°</i>	0.14 <i>0.161°</i>	0.14 <i>0.235°</i>	0.13 <i>0.383°</i>	0.13 <i>0.52°</i>	(6.85) <i>(6.85)</i>
Sodium lauryl sulfate U.S.P.	0.10 <i>0.029°</i>	0.08 <i>0.046°</i>	0.07 <i>0.068°</i>	0.05 <i>0.086°</i>
Sodium nafcillin	0.14 <i>0.039°</i>	0.14 <i>0.078°</i>	0.14 <i>0.158°</i>	0.13 <i>0.219°</i>	0.10 <i>0.285°</i>
Sodium oxacillin U.S.P.	0.18 <i>0.050°</i>	0.17 <i>0.095°</i>	0.16 <i>0.177°</i>	0.15 <i>0.257°</i>	0.14 <i>0.408°</i>	0.14 <i>0.52°</i>	(6.64) <i>(6.64)</i>
Sodium phenylbutazone	0.19 <i>0.054°</i>	0.18 <i>0.104°</i>	0.17 <i>0.202°</i>	0.17 <i>0.298°</i>	0.17 <i>0.488°</i>	0.17 <i>0.52°</i>	(5.34) <i>(5.34)</i>
Sodium sulfobromo- phthalein U.S.P.	0.07 <i>0.019°</i>	0.06 <i>0.034°</i>	0.05 <i>0.060°</i>	0.05 <i>0.084°</i>	0.04 <i>0.123°</i>
Sodium warfarin U.S.P.	0.18 <i>0.049°</i>	0.17 <i>0.095°</i>	0.16 <i>0.181°</i>	0.15 <i>0.264°</i>	0.15 <i>0.430°</i>	0.15 <i>0.52°</i>	(6.10) <i>(6.10)</i>
Theophylline sodium glycinate N.F.	0.32 <i>0.090°</i>	0.31 <i>0.180°</i>	0.31 <i>0.355°</i>	0.31 <i>0.52°</i>	(2.94) <i>(2.94)</i>
Thiethylperazine maleate	0.10 <i>0.030°</i>	0.09 <i>0.050°</i>	0.08 <i>0.089°</i>	0.07 <i>0.119°</i>	0.05 <i>0.153°</i>
Thiopropazate DiHCl	0.20 <i>0.053°</i>	0.16 <i>0.090°</i>	0.12 <i>0.137°</i>	0.10 <i>0.170°</i>	0.08 <i>0.222°</i>
Thioridazine HCl	0.06 <i>0.015°</i>	0.05 <i>0.025°</i>	0.04 <i>0.042°</i>	0.03 <i>0.055°</i>	0.03 <i>0.075°</i>
Trifluoperazine DiHCl	0.18 <i>0.052°</i>	0.18 <i>0.100°</i>	0.13 <i>0.144°</i>
Trimeprazine tartrate	0.10 <i>0.023°</i>	0.06 <i>0.035°</i>	0.04 <i>0.045°</i>	0.03 <i>0.052°</i>	0.02 <i>0.061°</i>
Trimethadione U.S.P.	0.23 <i>0.069°</i>	0.23 <i>0.133°</i>	0.22 <i>0.257°</i>	0.22 <i>0.378°</i>	...	0.21 <i>0.52°</i>	(4.22) <i>(4.22)</i>
Tropicamide	0.10 <i>0.030°</i>	0.09 <i>0.050°</i>
Trimethobenzamide HCl N.F.	0.12 <i>0.033°</i>	0.10 <i>0.062°</i>	0.10 <i>0.108°</i>	0.09 <i>0.153°</i>	0.08 <i>0.232°</i>
Valethamate bromide	0.16 <i>0.044°</i>	0.15 <i>0.085°</i>	0.15 <i>0.168°</i>	0.14 <i>0.238°</i>	0.11 <i>0.324°</i>
Vancomycin HCl U.S.P.	0.06 <i>0.015°</i>	0.05 <i>0.028°</i>	0.04 <i>0.049°</i>	0.04 <i>0.066°</i>	0.04 <i>0.098°</i>
Xylometazoline HCl	0.22 <i>0.065°</i>	0.21 <i>0.121°</i>	0.20 <i>0.232°</i>	0.20 <i>0.342°</i>	...	0.19 <i>0.52°</i>	(4.68) <i>(4.68)</i>

^a The values first listed for the chemical substances are NaCl equivalents. ^b The second values, in *italics*, are freezing point depression values in °C. ^c The percentage concentration (w/v) at isotonicity is given in parentheses in the last column. ^d The official designations refer to U.S.P. XVII and N.F. XII.