Surface Activity and Wetting Effect of Artificial Tear Preparations

L. V. Chasovnikova, V. E. Formazyuk, V. I. Sergienko, and Yu. F. Maichuk

UDC 615.362.847.036

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 115, № 4, pp. 368–370, April, 1993
Original article submitted December 3, 1992

Key Words: *cornea; surface tension; natural tears; artificial tear preparation; contact wetting angle*

Good wettability of the corneal epithelium in health is provided by two properties of natural tears. First, tears contain high concentrations of mucin, a glycoprotein, which is adsorbed on the external surface of the corneal epithelium and makes it hydrophilic. Second, natural tears are characterized by a relatively low surface tension (40-46 mN/m) [4,6], this improving their wetting action in comparison with water. The external corneal surface washed free with detergents of the tear components adsorbed on it shows hydrophobic properties [6]. Its critical surface tension assessed by Zisman's method [8] is equal to 28 mN/m, due to which this surface is very poorly wetted with water. The equilibrium contact angle (θ) for a water drop placed onto it is equal to 81° [3]. In health a lacrimal fluid drop spreads well over the external corneal surface (θ=20°) [3]. Patients in need of artificial tear preparations may be tentatively divided into two groups. Some patients suffer from lacrimal gland hypofunction. Other patients with normal lacrimation may have for some reason (for example, because of injuries inflicted with contact lenses) impaired mucinous coating of the cornea, this resulting in the exposure of the epithelial hydrophobic sites and lack of moistening of the external surface of the eye with tears. This may eventually lead to the destruction of epithelial cells.

Research Institute of Physicochemical Medicine, Ministry of Health of Russia, Moscow (Presented by Yu. M. Lopukhin, Member of the Russian Academy of Medical Sciences)

The present study included measurements of the surface tension of fourteen artificial tear preparations, for it is this parameter that determines the pharmacological effect of such drugs, and the assessment of these agents' ability to spread over the surface of paraffin.

MATERIALS AND METHODS

The artificial tear preparations enumerated in Table 1 were used in the form of the ready-made product. Natural tears (not more than 0.1-0.2 ml) were collected from healthy subjects with a micropipette from the inferior transitional fold of the eyeball conjunctiva. Paraffin was chosen as the model of exposed corneal epithelium because its surface energy (32 mN/m) is close to that of corneal surface free of mucin. The findings were compared with similar characteristics of natural tears of normal subjects. The surface tension (σ) of artificial and natural tear solutions was measured by Wilhelmi's method within an accuracy of 0.2 mN/m. The procedure was as follows. A wet Wilhelmi's slide prepurified with hot chromium mixture was suspended on a quartz spiral above a round 20 ml cuvette. Distilled water was poured into the cuvette so that the slide touched its surface. the depth of submersion of the plate in the water was fixed using a microscope. If the σ value calculated from the value of the slide sinking in the water was close to the reference value (72.2±0.2 mN/m), a fixed volume (0.5-300 µl) of artificial or natural tears was added to the water with

0007-4888/93/0004-0387$12.50

TABLE 1. Minimal Equilibrium Surface Tension of Artificial and Natural Tear Solutions (σ_{min}) and Contact Wettability Angles (θ) of Undiluted Tears on Paraffin

№ of agent	Name	Country of manufacture	$\sigma_{e\ min}$, mN/m	$\theta°$
1.	Adapt	Canada	55.2	83.5
2.	Conta 7	France	58.2	86.7
3.	Contafilm	Germany	55.0	82.9
4.	Dialens	USA	56.6	91.7
5.	Hypo Tears	USA	49.2*	67.7**
6.	Lacrisifi	Spain	47.8*	81.6
7.	Lacrisin	Czechoslovakia	47.8*	81.4
8.	Murine Plus	USA	48.0*	59.8**
9.	Tears Naturale	USA	46.4*	52.1**
10.	Tears Naturale II	USA	45.4*	83.5
11.	Kauglyukin	Russia	69.4	93.3
12.	Lakrikin	Russia	69.0	93.8
13.	Lakrimal	Poland	54.0	63.4**
14.	Laktron	Russia	63.0	65.4**
15.	Natural tears		47.5±1.5	78.2
16.	Distilled water		72.2	106.6
17.	Methylene iodide			54.1

Note: explanations for asterisks in the text.

a syringe. The slide was then pushed out of the water because of a reduction of σ which resulted from the formation on the water surface in the cuvette of a layer of lacrimal surface-active components, and the course of this pushing out was followed up. The solution was gently stirred with a magnetic stirrer over the course of the follow-up. σ was considered to have attained equilibrium value if the measuring slide position remained unchanged for 15-20 min. This equilibrium value (σ_e) was designated as the lacrimal surface tension at a certain dilution. The wetting contact angles were measured by the sitting droplet method under a horizontal microscope fitted with a goniometric ocular in a device described previously [8]. The contact angles for each agent were recorded for 15-20 droplets and the mean value calculated. Paraffin-coated slides were used as a bottom plate. For its preparation, the slides were embedded in melted paraffin and then air-dried.

RESULTS

Measurements of surface tension using our device require high liquid volumes, which we do not have. It is also quite impossible to have natural tears in such volumes. Our previous research had demonstrated that the σ values of diluted natural tears are sufficiently similar to those of undiluted tears. A similar method was used in the present research. To assess the surface tension of undiluted drugs simulating natural tears, we measured the surface tension of diluted preparations. The most significant components of these agents are surface-active high polymers: cellulose ethers, dextran, polyvinyl alcohol, polyvinyl pyrrolidone, etc. The dilution of concentrated polymer solutions to a certain critical concentration does not involve a surface tension increase [1] because the counts of polymer molecules in the solution are sufficient to form a monomolecular layer determining the measured σ value. By measuring the surface tension of artificial tear solutions of various concentrations, we revealed that the maximal reduction of this parameter is attained at sufficiently high dilutions of the drugs. It is clearly seen in Fig. 1, which presents the relationship between σ and the dilutions of all fourteen artificial tear preparations we examined. A similar relationship for artificial tears is presented on the scheme for comparison. It may be seen that all the drugs contain surfactants, and therefore when small amounts are administered, the solution surface tension is in proportion to the drug concentration. The curve plateau indicates the attainment of the surface tension reduction maximally possible for a preparation (σ_{min}). The drugs examined differ greatly from each other both in their capacity to reduce water surface tension and in the solution concentrations at which threshold σ values are attained. The surfactants in the composition of artificial tears should show a tendency to be absorbed on the external surface of the ocular epithelium and, this in turn should result in improved surface wetting. On the basis of the σ measurements, drugs whose surface tension is close to or less than that of natural tears are to be preferred. When instilled into the eye, they will not increase the surface tension of the patient's tears mixing with them. Their capacity for film formation on the corneal epithelium can be expected to be at least as good as that of natural tears. Six of

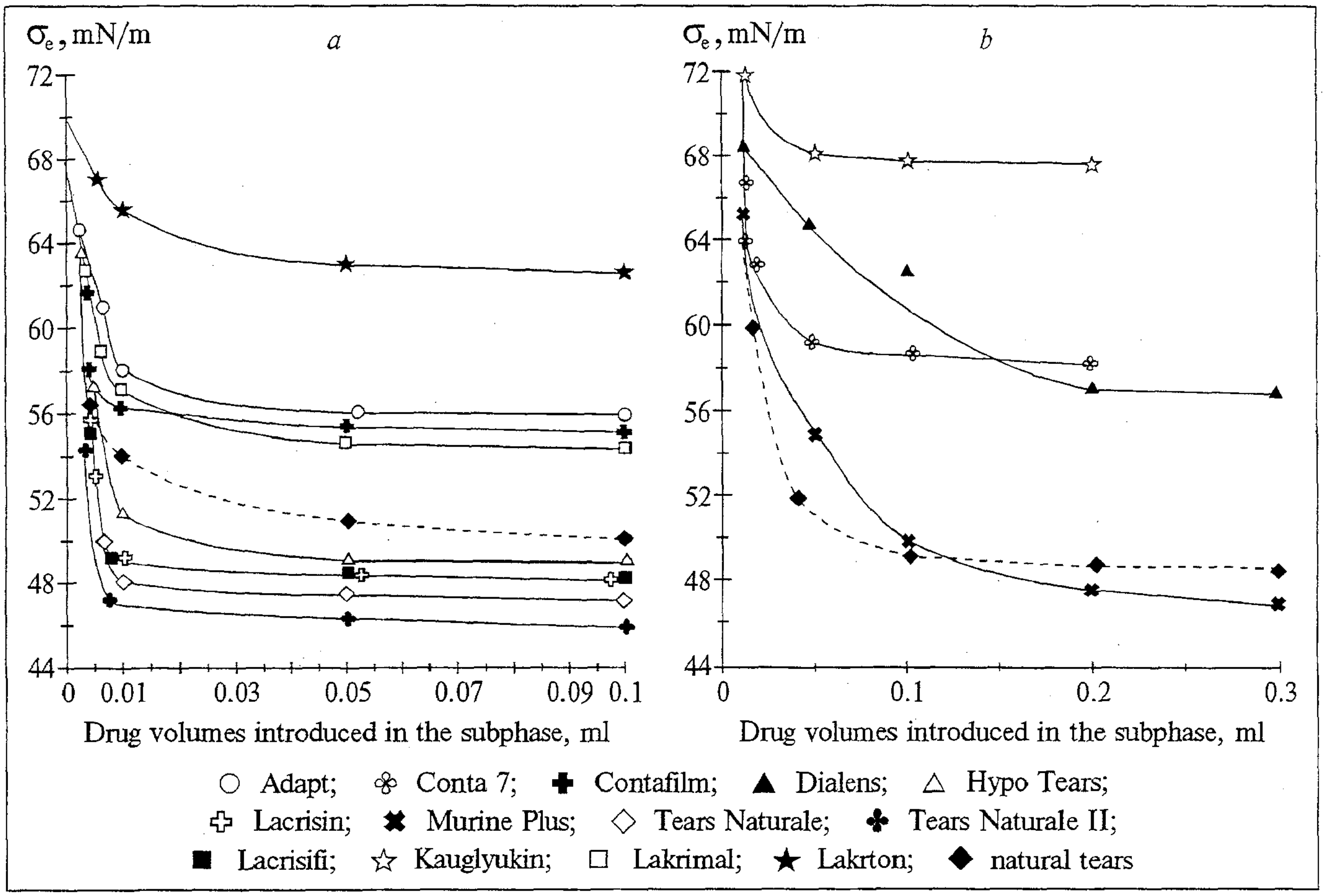

Fig. 1. Relationship between σ_e and dilution of artificial and natural tears.

the tested agents met these requirements, Nos. 5-10 in the table, marked with an asterisk. The next step of our study was to check whether these preparations really wet the hydrophobic surface to the optimal degree. The surface energy of the paraffin used by us was assessed from water and methylene iodide contact angles by the Fowkes-Owens-Wendt method [7] and found equal to 32 mN/m. The contact angles of wetting of undiluted artificial and natural tears on this surface were measured (results given in Table 1). Natural tears with a contact angle (θ) of 78.2° poorly wet the cornea of a dry eye; hence, when treating patients with such symptoms the physician should prescribe drugs wetting paraffin better than natural tears. Five agents are characterized by such properties; Nos. 5, 8, 9, 13, and 14, marked with two asterisks in the table. Only three of these, Nos. 5, 8, and 9, had $\sigma_{e\ min}$ lower than that of natural tears. A possible cause of this difference is that, with the reduction of surface tension and wettability used as the basic criterion, a considerable decrease of the surface tension of agents Nos. 6, 7, and 10 was attained mainly at the expense of the high surface activity of low-molecular preservatives, but, as was previously demonstrated [2], even less surface-active polymers forming hydrophilic layers at the interface between liquid and solid matter may provide better wetting of a solid surface than low-molecular surfactants. This seems to explain the good wetting effect of agents Nos. 13 and 14. The capacity to wet thoroughly a hydrophobic surface being a more objective criterion of the quality of an artificial tear preparation, the agents marked with two asterisks are to be preferred in cases with suspected poor wettability of the cornea. For patients with inadequate function of the lacrimal glands any artificial tear preparations are obviously indicated.

REFERENCES

1. Yu. S. Lipatov, *Colloid Chemistry of Polymers* [in Russian], Kiev (1984), pp. 54-56.
2. V. M. Rudoi, B. G. Aristov, N. G. Sarygina, *et al.*, *Zh. Fiz. Khimii*, **57**, № 9, 2279-2282 (1983).
3. F. Y. Holly and M. A. Lemp, *Exp. Eye Res.*, **11**, 239-250 (1971).
4. F. Y. Holly, Y. T. Patten, and C. N. Dohlman, *Ibid.*, **24**, 479-491 (1977).
5. F. Y. Holly, *Invest. Ophthal.*, **17**, 552-557 (1978).
6. D. Miller, *Arch. Ophthal.*, **82**, 368-371 (1969).
7. D. K. Owens and R. C. Wendt, *J. Appl. Polym. Sci.*, **13**, № 8, 1741-1748 (1969).
8. W. A. Zisman, *Contact Angle, Wettability, and Adhesion*, Ed. F. M. Fowkes, Washington (1964), p. 15.