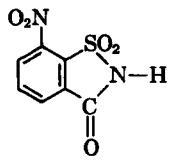
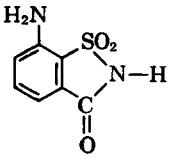
Permanganate oxidation of 6-nitro-*o*-toluenesulfonamide gave 7-nitrosaccharin (II). Reduction of 7-nitrosaccharin by hydrogen with palladium-on-carbon catalyst yielded 7-aminosaccharin (III).



II



III

The 7-nitrosaccharin is essentially tasteless, while 7-aminosaccharin has a sweet taste.

EXPERIMENTAL[1]

7-Nitrosaccharin.[2]—This compound was prepared by alkaline potassium permanganate oxidation of 6-nitro-*o*-toluenesulfonamide by the method used by Noyes (4) to synthesize 6-nitrosaccharin. The 6-nitro-*o*-toluenesulfonamide, m.p. 201–202° [reported m.p. 197–199° (3)], was synthesized according to the series of reactions shown above. Recrystallization of the 7-nitrosaccharin from ethanol gave yields of approx. 25% of yellowish-white crystals, m.p. 262–264° dec. Approx. 30% of unreacted starting sulfonamide was recovered and used in succeeding oxidations.

Anal.[3]—Calcd. for $C_7H_4N_2O_5S$: C, 36.84; H, 1.77. Found: C, 37.02; H, 1.86.

7-Aminosaccharin.—Reduction of 7-nitrosaccharin using hydrogen with palladium-on-carbon catalyst according to standard procedures (5), followed by recrystallization of the product from ethanol gave crystalline 7-aminosaccharin (82%) m.p. 269–270°. Dilute solutions of the compound in ethanol displayed a bluish fluorescence.

Anal.—Calcd. for $C_7H_6N_2O_3S$: C, 42.42; H, 3.12. Found: 42.49; H, 3.09.

[1] Melting points were performed by the capillary tube method and are uncorrected.

[2] *Chem. Abstr.* nomenclature: 7-nitro-1,2-benzisothiazolin-3-one-1,1-dioxide.

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[3] Analyses were performed by Elek Micro Analytical Laboratories, Los Angeles, Calif.

Polytetrafluorethylene Tipped Tablet Punches

By SHELDON SIEGEL†, EDWARD J. HANUS, and JOHN W. CARR

Severe powder sticking to tablet punch surfaces during the production of an effervescent tablet has been overcome by the utilization of punches tipped with polytetrafluorethylene.[1]

The objective of this investigation was to develop an effervescent tablet containing a mixture of sodium isoascorbate and isoascorbic acid which would be rapidly soluble in water and form a solution completely free of turbidity. This tablet was to be used as a source of isoascorbate for meat curing processes to provide a convenient measure for the meat packer who wished to equate his antioxidant requirements to numbers of tablets in preference to units of weight or volume.

The manufacture of an effervescent tablet which yields a clear solution when dissolved in water is not possible when conventional tablet lubricants such as the metallic stearates, mineral oil, etc., are used. For this reason polyethylene glycol 4000 was chosen to act in the dual role of binder and water soluble lubricant. An effervescent tablet blend was prepared and compressed directly on a Stokes model DDS-2 tablet machine into 15-Gm. wafers having a diameter of $1^5/_{16}$ in. The blend had the following composition (1):

Sodium isoascorbate	9.92	Gm./tablet
Isoascorbic acid	2.02	"
Sodium bicarbonate U.S.P. powder	1.06	"
Citric acid anhydrous U.S.P. powder	0.50	"
Polyethylene glycol 4000 (100 mesh)	1.50	"
	15.00	"

When direct compression of this powdered formulation was attempted, severe picking and sticking occurred after compressing relatively few tablets; satisfactory production was impossible because of frequent breakdowns. As an outgrowth of this investigation the utilization of plastics, as components of tablet punches, was studied.

EXPERIMENTAL

Circles of polyethylene film were cut from a plastic bag and bonded to punch faces with a rubber cement. Satisfactory experimental facsimilies of the desired formulation were produced with these punches on a single punch Stokes model F tablet machine. It was noted that the sticking and picking observed in earlier experiments was significantly reduced. Polytetrafluorethylene (2–4) was subsequently investigated because of its inherent self-

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[1] Marketed as Teflon by E. I. duPont de Nemours and Co., Inc., Wilmington, Del.

lubricating property. Polytetrafluorethylene tablet punches were prepared from $^{5}/_{8}$-inch rods and used in conjunction with a $^{5}/_{8}$-inch metal die on the single punch machine. Sticking and picking were almost completely eliminated, but the operation was complicated by the tendency of this plastic to deform under pressure (a phenomenon known as "cold flow"). The punch area that entered the die retained its shape, but the shaft of the punch was deformed and buldged outwards. It was then reasoned that if faces of metal punches were tipped or coated with polytetrafluorethylene, the plastic would be confined within the die cavity during compression, thus preventing deformity. Coating the punch by spraying a thin layer of polytetrafluorethylene was somewhat effective; however, on extended tableting runs the material peeled off. Punches for the single punch machine were subsequently modified by bonding a small polytetrafluorethylene tip to the surface. The tableting operation using the latter punches was quite satisfactory and similar punches were modified and successfully used for the larger production equipment. The use of this device has eliminated much of the difficulty previously experienced with the manufacture of this product.

Several disadvantages were observed during the use of polytetrafluorethylene tipped punches. They are easily damaged and are subject to tip deformity and breakage. Because of the tendency of this plastic to deform under pressure, only flat faced or at most a slightly beveled tablet can be produced with these punches. Monogramming is obviously not practical. Nevertheless, for our specific problem polytetrafluorethylene tipped punches performed satisfactorily under production conditions.

Bonding Polytetrafluorethylene to Punch Surfaces.—Polytetrafluorethylene is not easily bonded to metal surfaces and requires a series of operations to produce a firm seal. An accepted procedure to facilitate bonding is to etch the surface of the plastic with molten sodium and cement it under high pressure to the metal surface by means of an epoxy resin cement. Tipped punches prepared in this manner were satisfactory but were subject to cleavage of the plastic component from the metal surface after a period of use. Modification of the bonding technique by first spraying the punch surface with a layer of pure molybdenum in order to produce a rough surface for greater plastic adherence significantly reduced this breakage (5).

SUMMARY

A method has been developed for preparing by direct compression a large effervescent tablet containing a mixture of sodium isoascorbate and isoascorbic acid which dissolves to form a solution free of turbidity or haze. The use of tablet punches tipped with polytetrafluorethylene has successfully circumvented the major problem of sticking and picking associated with the manufacture of this product.

The utilization of polytetrafluorethylene tipped punches may find application in other tablet formulations exhibiting similar difficulties. In addition, preliminary experimentation with this device has been successful in reducing lubricant levels in certain tablet blends and further investigation in this area is warranted.

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Communications

Inactive Prednisone Tablets U.S.P. XVI

Sir:

We wish to report a case in which prednisone tablets meeting U.S.P. XVI specifications were found to be clinically inactive *in vivo* and some *in vitro* test results which suggest a possible reason for their inactivity.

A 25-year-old white married female of Mediterranean ancestry has been under the care of one of us (FAC) for approximately 5 years. Her clinical diagnosis was familial Mediterranean fever with repeated episodes of clinical peritonitis confirmed by laboratory studies and previous surgical exploration. The prompt use of oral prednisone in amounts of 20 mg. in a 24-hour period for the first 2 or 3 days would promptly abort the clinical symptoms, the laboratory findings of leukocytosis, etc., changing only slightly. The patient's prescriptions had been written with the generic name "prednisone." On one occasion, after 72 hours of 5 mg. four times a day, the patient had no clinical effects from the medication. It was discovered at that time that a different "brand" of prednisone had been dispensed than that previously used. The patient was immediately transferred to the brand of prednisone used previously and again within 24 hours there was almost complete resolution of the clinical syndrome.

The manufacturer's reassay of tablets, from the same lot as the tablets which were ineffective in treatment of the condition described, indicated that they contained essentially all of their labeled content. Also, the tablets passed the