

NEW THERAPEUTIC USES FOR WELL-KNOWN CHEMICALS.*

BY E. FULLERTON COOK.

Benzyl Benzoate.

In an extensive study of the action of opium alkaloids, David I. Macht, M.D., of the Pharmacologic Laboratory of Johns Hopkins University, has demonstrated that these alkaloids divide into two classes of which morphine is the most important of those belonging to the pyridin-phenanthrene group and papaverine the principal representative of the benzyl-isoquinoline group.

The morphine group, including codeine, or methyl-morphine, dionine or ethyl-morphine, heroin or diacetyl-morphine, apomorphine, apocodeine, eucodine or methyl-codeine, paracodine or dihydrocodeine, and codeonal or codeine diethyl-barbiturate, all tend to stimulate the contractions and heighten the tonus of smooth muscles, but papaverine, or its related alkaloids narcotine, narceine, and hydrastine, all produce an inhibition of the contractions of smooth muscles and lower their tonus.

He also fully proves that this action of the papaverine group was due to the benzyl portion of the molecule and this led to an effort to find a non-narcotic benzyl combination which would produce similar therapeutic action and resulted in the discovery that the esters, benzyl acetate and benzyl benzoate possessed such properties.

This was first shown by experiments upon animals and subsequently by many clinical tests and has led to the suggested use of the latter where antispasmodic action upon the smooth muscles is desired.

It was found that while the acetate was of equal therapeutic value it produced slight irritation upon the stomach and the benzoate has, therefore, been recommended for general trial. It is employed in dysentery, biliary, renal and uterine colic, in arterial spasms, bronchial spasms, as in asthma, in dysmenorrhoea and other excessive spasms of smooth muscles.

Benzyl benzoate has long been used as a solvent in perfumery, especially for synthetic musk, and also for the incorporation and fixing of the flavor in chewing gum, where it prevents loss by evaporation during the heating and kneading of the mass, and it is interesting to learn that its therapeutic value was suggested by chemical and physiological experiments, conducted in a modern research laboratory, whereby the value of such work is again conclusively demonstrated.

Pharmaceutically, benzyl benzoate must be treated very much like an oil. Its dose is small, 2 to 5 minims, and it has been most largely administered in 20 percent alcoholic solution containing 2 percent of soap which makes a solution that is readily miscible with water. It has also been dissolved in fixed oil and dispensed in capsules. Dr. Litzenberg¹ suggests the following prescription for its administration for dysmenorrhoea:

℞— Benzyl Benzoate.....	10 mils
Mucilage of Acacia.....	5 mils
Aromatic Elixir of Eriodictyon, to make.....	50 mils
Give from one-half to two teaspoonfuls as necessary.	

* Read before Philadelphia Branch, A. Ph. A., November meeting, 1919.

¹ *Jour. A. M. A.*, 73, 601, 1919.

In the *Jour. A. M. A.*, Vol. 73, p. 599 and p. 601, a more extensive review and many additional references may be found.

Benzyl Alcohol (Phenmethylol).

During experimental work on benzyl combinations, in the study of their anti-spasmodic action, Dr. David I. Macht (Pharmacologic Laboratory of Johns Hopkins University) incidentally tasted a minute quantity of benzyl alcohol and discovered that his tongue was completely anesthetized by it, the numbness, coolness and hardness, similar to the action of cocaine, continuing for over two hours.

This accidental discovery was followed by numerous experiments on animals and subsequently in minor operations and dentistry, with results that compare favorably with any of the known local anesthetics and in some respects greatly to the advantage of the benzyl alcohol.

Fortunately benzyl alcohol is soluble in water and normal salt solution to the extent of 4 percent and this is sufficiently strong for use as a local anesthetic by injection. When used as an anesthetic in from 1 to 4 percent solutions in normal salt, it has never been found to cause any marked irritation or destruction of tissue, certainly less than that produced by equivalent amounts of cocaine or quinine and urea hydrochloride solutions.

The solutions may be sterilized by boiling without causing decomposition or loss of benzyl alcohol. When used on the eye it was found desirable to add a small amount of epinephrin (1 in 20,000) thus avoiding all irritation. A comprehensive study of its anesthetic and pharmacologic action will be found in the *Journal of Pharmacology and Experimental Therapeutics*, 1918, p. 263.

Solution of Zinc Chloride.

William Wayne Babcock, Lieutenant Colonel in the Medical Corps of the United States Army, stationed at General Hospital No. 6, Fort McPherson, Georgia, has recently reported the successful use of solution of zinc chloride (prepared by saturating U. S. P. hydrochloric acid with zinc) in the treatment of chronic infected wounds of soft tissue and also of bone involvement.

The patients were all returned from the war areas and had already received months of treatment, usually with Dakin's solution, and been operated upon at least several times. The wounds showed a variety of infecting micro-organisms, and the solution of zinc chloride was used as a sterilizing agent; the tissue, which it simultaneously destroyed, being completely removed as a part of the operation. This procedure permitted the immediate closing of wounds, the avoiding of painful dressings, and a large percentage of permanent recoveries.

The technique is as follows, the operation being conducted under local or general anesthesia:

Wound Preparation.—The wound areas having previously been thoroughly cleansed by daily washing and shaving, the skin is thoroughly scrubbed with a solution consisting of 2 parts of compound solution of cresol, 10 parts of oil of turpentine and 88 parts of gasoline, and then painted with 3 percent tincture of iodine.

Wound Sterilization.—Immediately after the cleansing, the sinuses, cavities and wound surfaces are sterilized by the use of the solution of zinc chloride, injecting

it under pressure, or packing with cotton pledgets, dipped in the solution, and great care is taken to see that all unhealed and granulating surfaces are reached.

The time of five minutes is allowed for the penetration of the zinc solution, and if it has been injected, under pressure, into bone sinuses, a tourniquet must be applied and the solution allowed to enter the circulation only slowly, otherwise collapse will result. Because of the caustic character of this solution and the danger of direct introduction into the circulation it cannot be used in fistulas connected with the bladder, or intestine, nor can it be used in the presence of erysipelas, or other acute spreading infection.

Color Delineation.—At the end of five minutes, the following solution is applied, in the same manner as the zinc chloride solution:

Saturated Alcoholic Solution of Methylene Blue.....	20
Potassium Hydroxide.....	3
Phenol.....	5
Ether, sufficient to make.....	100

When this solution evaporates it leaves the exposed granular surfaces dark blue-black, dry bloodless on manipulation, and sterile, and beneath a grayish white tissue which has been sterilized and devitalized by the zinc chloride.

Excision of Infected Area.—The entire diseased area is now removed, the wound closed, and a moist, non-irritating, antiseptic dressing applied for the first week, or until all tissue reaction has subsided. The solution used consists of:

Hydrated Chloral.....	1
Alcohol.....	10
Glycerin.....	25
Saturated solution of boric acid.....	65

This is injected into the gauze dressings every two or four hours by means of rubber tubes which are inserted when the dressing is applied.

The part where the operation occurred should be kept quiet, elevated, and warm, and there should be no probing, squeezing, or introduction of tubes. The dressings should be changed daily and the adjacent skin must be kept clean and coated with a 2 percent yellow mercuric oxide ointment.

NOTE.—The details of this treatment and formulas have been taken from a report on the subject read by Dr. Babcock at the recent meeting of the American Medical Association but not yet published.

ALCOHOL IN THE PHARMACOPOEIA.*

BY HENRY KRAEMER.

The study of the use of alcohol in Pharmacy has engaged the master minds in our profession. It is more than 50 years ago that Dr. E. R. Squibb¹ in one of his classical papers discussed the subject of "the proposed economy of alcohol in percolation, as applied to the extracts and fluidextracts of the Pharmacopoeia." He called attention to the fact that "the increase in the price of alcohol since the last revision of the U. S. Pharmacopoeia has materially interfered with the use of the officinal extracts and fluidextracts by the greatly increased cost of preparing

* Read before Scientific Section, A. Ph. A., New York meeting, 1919.

¹ Proc. A. Ph. A., 1865, p. 201.