

1

2

3,536,809

**MEDICATION METHOD**

Norman Applezweig, New York, N.Y., assignor to Alza Corporation, Palo Alto, Calif., a corporation of California

No Drawing. Continuation-in-part of application Ser. No. 492,301, Oct. 1, 1965. This application Feb. 17, 1969, Ser. No. 799,910

Int. Cl. A61j 7/00; A61k 9/00, 17/00

U.S. Cl. 424—28

4 Claims

**ABSTRACT OF THE DISCLOSURE**

A method of administering medication employs a strip covering the medicament which is inserted between the gum and cheek so that absorption of the medicament at a predetermined interval through the buccal mucosa into the bloodstream may take effect, after which the strip is removed and discarded.

The present invention relates generally to improvements in the administration of medicaments and it relates more particularly to an improved method for introducing a medicament into the blood stream. This application is a continuation in part of application Ser. No. 492,301, filed Oct. 1, 1965 now abandoned.

The conventional methods of introducing a medicament into the blood stream are by direct injection and by oral administration, in the latter case the medicament being absorbed through the membrane which lines the passage of the medicament. Many medicaments are completely ineffective or of radically reduced efficacy when orally administered since they either are not absorbed or are adversely affected before entering the blood stream and thus do not possess the desired activity. On the other hand, the direct injection of the medicament into the blood stream, while assuring no modification of the medicament in administration, is a difficult, inconvenient and highly uncomfortable procedure and requires a high degree of skill.

Sublingual tablets and any other form of sublingual administration are subject to the limitations that there are smaller surfaces for the transmission through the mucosal membrane, that in the case of sublingual location a substance there placed causes salivation, and by reason of the additional fluid and the position in the mouth is likely to lead to swallowing of at least a portion of the medicament. Buccal tablets are known also but there are important drawbacks accompanying their use and they have enjoyed little success. In some instances larger dosages are required to be inserted in the buccal tablet than are needed in the case of the buccal strip of the present invention. In addition they usually take a great deal of time to deliver the medicament to the buccal surface. The buccal tablet also causes pressure between the lip and the gum, which may be uncomfortable and painful. This pressure also may cause the tablet to disintegrate and thus more of the contents are likely to be swallowed.

It is therefore a principal object of the present invention to provide an improved method for the introduction of medication into the blood stream.

A further object of the present invention is to provide an improved method for the administration of hormones.

The above and other objects of the present invention will become apparent from a reading of the following description in which examples are given merely by way of illustration and are not intended to limit the scope of the invention.

It has been found that certain medicaments when slowly released to the oral mucosa and particularly to the

buccal membrane are absorbed thereby and efficiently enter the blood stream and unexpectedly effect a highly superior therapy or activity. Thus, in a sense of the present invention contemplates the employment of a medication form for introducing a pharmaceutically active material into the blood stream for a predetermined period comprising a film or strip carrying a pharmaceutically active material releasable therefrom in an aqueous medium for absorption through the oral mucosa buccal tissue. In another sense the present invention involves the method of introducing a medicament into the blood stream comprising positioning a fibrous absorbent strip carrying a medicament releasable therefrom in overlying contact with the oral mucosa buccal tissue.

While the present method is employed to great advantage in the administration of hormones, for example, progesterone, estrone, testosterone, cortisol, desoxycorticosterone, it may be employed to advantage with other medicaments, for example, proteolytic enzymes such as trypsin, chymotrypsin, streptokinase, streptodornase, appetite depressants, antispasmodics and sedatives, where rapid entrance to the blood stream is highly desirable.

The base of the subject medication form or buccal strip is advantageously an absorbent web such as a strip of woven or non-woven fabric, filter paper or cotton gauze, and is of a dimension which may be comfortably retained between the gum and cheek of the subject and can support in a releasable form a sufficient dosage of the medicament to be administered. The buccal strip may be advantageously between one and ten centimeters long, for example five centimeters, and between one-half and three centimeters wide, for example, one centimeter.

The medicament may be carried by the buccal strip in its pure state or it may be admixed with suitable carriers which facilitate the support of the medicament by the buccal strip and its suitable release to the buccal face. Examples of such carriers are Carbowax, polyvinylpyrrolidone, carboxymethyl cellulose, gum arabic and other water soluble or dispersible thickening agents and adhesives.

As an example of a medication form, its preparation and use in accordance with the present invention, a piece of Pellon 2100 (100% Polyamide fiber) fabric was immersed in a 20% dispersion of progesterone in a molten mixture of 15% Carbowax 400 and 85% Carbowax 4000 to fully impregnate the fabric. The impregnated fabric was then allowed to cool. The progesterone carrying fabric is cut into one by two centimeter strips, each strip containing about 26 milligrams of progesterone.

In the administration of the progesterone in accordance with the present invention the subject merely places and retains the progesterone carrying buccal strip described above between the confronting faces of the gum and the cheek and in contact with the buccal membrane. The buccal strip releases the progesterone which directly enters the blood stream through the buccal membrane. The rate of release of the progesterone averaged about 2 mgm. minute and the buccal strip was substantially depleted of medicament in approximately 15 minutes. At the end of such period the strip is removed and discarded.

Subjects who were administered progesterone in dosages of 26 mg. at intervals of 24 hours for five days by the use of the buccal strip medication form in the manner set forth above had withdrawal bleeding two to five days following cessation of medication.

These were patients who suffered from a variety of menstrual difficulties and were not capable of spontaneous menstruation. Menstruation could be induced in such patients by intramuscular injection of 100 mg. of progesterone. Following intramuscular progesterone, withdrawal bleeding could be demonstrated after four to five days.