METHOD OF LOCATING ENTERIC CONSTRIC-
TIONS WITH A PLURALITY OF PILLS CONTAIN-
ING AN X-RAY CONTRAST AGENT

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1 Claim. (Cl. 167—95)

This invention relates to X-ray-opaque pills having a
controlled rate of disintegration in the stomach and in-
testines, thus being adapted to facilitate the location of
obstructions and the estimation of their severity.

An enteric obstruction in man or domestic animals is a
sudden, acute and highly dangerous condition which, un-
less quickly diagnosed and corrected, causes serious com-
plications or death. Such obstructions may be partial or
total and are difficult to locate by X-ray, especially when
only partial. The usual X-ray technique is to admin-
ister a slurry of barium sulfate or other X-ray-opaque
material and follow its movement through the body by
means of X-rays. Frequently, the stoppage is less than 100%
complete, in which case the slurry leaks past the
obstruction and thus fails to show where the latter is.

According to the invention, barium sulfate or other
X-ray-opaque material is mixed with methylcellulose
which may optionally contain hydroxyalkyl groups, and
then molded into a pill which when taken internally dis-
integrates at a controllable rate. The rate of disintegra-
tion depends primarily on the type and percentage of
methylcellulose used in the density of the pill. Thus, a
highly substituted, highly soluble, low viscosity methyl
cellulose dissolves faster than a lower substituted, high
viscosity methylcellulose. Similarly, a porous, low density
pill, molded under low pressure, dissolves faster than a
hard, dense pill molded under high pressure.

When desired, the time at which the disintegration of
the pill begins can be delayed for up to several hours after
it has been taken internally by coating the pill with a
protective coating of hydroxypropyl methylcellulose or, be-
ter, a mixture of hydroxypropyl methylcellulose and ethyl-
cellulose. Ethylcellulose being substantially insoluble in
water, its presence in the coating greatly reduces the sol-
bility of the latter and increases the time required for
disintegration of the pill. Thus, by controlling the
thickness of the coating and the percentage of ethylcellu-
lose therein, if any, one can control over a wide range the
initiation of and the rate of disintegration of the pill.

We generally prefer to keep the ratio of ethylcellulose to
hydroxypropyl methylcellulose in the range 1.3 to 3.1.
Lower ratios give quite rapid dissolution while higher ones
yield pills having unduly long dissolving times.

We have found it advantageous to plasticize the coatings
mentioned above in order to soften them and facilitate
their uniform dissolution. Any water-soluble non-toxic
plasticizer may be used, a suitable one being 1,2,3-tris-
(2-hydroxypropoxy)-propane.

When the pills of the invention are used to locate an
obstruction in the alimentary canal, a variety of tech-
niques may be used. Thus, a single large pill may be ad-
ministered and its progress followed by use of X-rays.
When it arrives at a blockage or a constriction too nar-
row to permit its passage, it stops and thus shows where
the obstruction is. If the obstruction is a constriction, the
pill is stopped until the process of dissoIution has reduced
its size to that which can pass the constriction. It then
passes the constriction. If this process is followed by X-
rays, not only the location but also the severity of the
constriction is apparent.

A quicker measure of the size of the free passage at a
constriction can be made by simultaneously administering
several pills of different sizes. Upon arriving at the con-
striction the smaller ones will pass through while the larger
ones will be held back, thus providing an accurate measure
of the size of the passageway.

The practice of the invention is illustrated by the follow-
ing examples. The viscosities shown for the cellulose
ethers were determined by the standard methods used in
the cellulose chemistry field.

Example 1

A mixture of barium sulfate (35%) and Methocel,
U.S.P., methylcellulose (65%) was molded in a spherical
die to make spheres of 0.5 inch diameter. These were
then coated by being dipped into a 10% solution in ben-
zeene-methanol (1:1) of 50 parts of ethylcellulose-medium,
50 cps; 30 parts of hydroxypropyl methylcellulose (30
cps, 6% 2-hydroxypropoxy, 28% methoxy by weight;)
and 20 parts of tris(2-hydroxypropoxy) propylamine.
The pills prepared as above required one hour to begin
disintegrate in an aqueous medium at room tempera-
ture. When administered to a dog they were easily fol-
lowed by X-ray observation and were sharply outlined
and hence easily measured. Disintegration began after
one hour, when the coating had been dissolved, and was
substantially complete in another hour.

Example 2

A pill identical to that of Example 1 was prepared ex-
cept that the ratio of ethylcellulose to hydroxypropyl
methylcellulose was increased from 50:30 to 55:25. This
coating required 2 hours instead of 1 hour to dissolve.

The coating on the pill is optional and is omitted when
it is desired that the pill begin dissolving sooner or dis-
solve at a higher rate.

The methylcellulose used as a binder for the barium
sulfate should contain about 27.5 to 32.0% of methoxyl
groups (by weight), its viscosity or molecular weight being
relatively unimportant. Also, it may optionally con-
tain up to about 15% of hydroxyalkyl groups containing
2 to 3 carbon atoms each; that is, hydroxyethyl, or 2- or 3-
hydroxypropyl groups. Such hydroxyalkyl groups improve
the moldability and cohesion of the barium sulfate pill
composition.

The ratio of cellulose ether to barium sulfate in the pill
may be varied widely, it being only necessary to use suffi-
cient ether to form a strong, coherent pill on the one hand
and enough barium sulfate to insure the pill showing ade-
quate X-ray contrast on the other. For general use, it
is preferred that the barium sulfate constitute about 25
to 50% by weight of the pill-forming composition.

I claim:

A method for locating and gauging an enteric constric-
tion comprising administrating orally a plurality of enteric
pills comprising barium sulfate and, as a binder there-
for, a water-soluble cellulose ether wherein the etherifying
radical is a member selected from the group consist-
ing of methyl, hydroxyethyl and hydroxypropyl radicals
and mixtures thereof, the combined content of hydroxy-
ethyl and hydroxypropyl radicals not exceeding about
15%, by weight, of said ether, said pills being substantially
spherical and of widely different diameters; tracking the
pills by means of X-rays; locating the constriction by not-
ing where the larger pills are stopped and gauging the size
of the constricted passage by noting the size of the largest
pills that pass through it.

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