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REDUCTION OF INTRAOCULAR PRESSURE

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No Drawing. Continuation-in-part of application Ser. No. 496,170, Oct. 14, 1965. This application July 20, 1967, Ser. No. 654,715

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ABSTRACT OF THE DISCLOSURE

This invention relates to the reduction of intraocular pressure and more particularly to the treatment of patients, for example those suffering from glaucoma or preoperatively to reduce intraocular tension prior to cataract surgery, e.g. intracapsular cataract extraction so as to facilitate the operative procedure, by the administration to the patent requiring the reduction of intraocular pressure of certain new and safe osmotic agents which have this effect. The agents of the present invention can be administered orally for the reduction of intraocular pressure, and these agents are marked by a high degree of effectiveness and complete lack of toxicity and lack of undesired side effects.

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of application Ser. No. 496,170, filed Oct. 14, 1965, now abandoned, for "Treatment of Epilepsy, Glaucoma and Constipation," which in turn is a continuation-in-part of application Ser. No. 405,829, filed Oct. 22, 1964, for "Treatment of Epilepsy and Glaucoma," now abandoned.

BACKGROUND OF THE INVENTION

Excessive intraocular pressure is a condition which manifests itself in certain abnormal eye conditions, and this is a problem of which opthalmologists are well aware. As a matter of fact, glaucoma is often defined as a pathologic state in which the intraocular pressure is elevated, intermittently or constantly, to a level which the eye cannot withstand without damage to structure or impairment of function. Reduction of intraocular pressure to a normal state is therefore an obvious desiderata in the treatment of glaucoma.

It is also desirable for the opthalmologist to try to lower ocular tension not only in the medical treatment of glaucoma but also prior to surgical treatment. Also, in the case of intracapsular cataract extraction it is desirable to reduce the intraocular pressure prior to the surgery.

Among the drugs which have been used for this purpose are acetazolamide (Diamox) and glycerine.

Both Diamox and glycerine when administrated orally have been found to cause vomiting or nausea and therefore the use of these substances has been limited. However, their need is present because the substances lower the intraocular pressure which permits the iris sphincter to regain its responsiveness to the use of miotics. The reduction of intraocular pressure is also important in diagnosis and prognosis because it may permit visibility of the fundus and evaluation of the visual prognosis, as well as a possibility of observing the condition of the angle obstruction.

The need for an efficient and safe osmotic agent to provide reduction in intraocular pressure is therefore quite apparent.

SUMMARY OF THE INVENTION

Generally speaking, the present invention relates to a method of reducing intraocular pressure, which comprises administering to a patient requiring such reduction of intraocular pressure a substance selected from the group consisting of polyglycerols, polyglycerol fatty esters, polyethylene glycols wherein "poly" is at least "tri," polypropylene glycols wherein "poly" is at least "tri," mixed polymers of propylene oxide and ethylene oxide, and mixed polymers of ethylene oxide and 1-amino-2-hydroxyethanol.

It is a primary object of the present invention to provide compositions and treatments for reduction of intraocular pressure with safety from the standpoint of toxicity and lack of undesired side effects.

It is another object of the present invention to provide compositions and treatments for reducing intraocular pressure permitting the use thereof in the treatment of glaucoma and other conditions requiring reduced intraocular pressure by oral administration of safe and effective substances.

Other objects and advantages of the present invention will be apparent from a further reading of the specification and of the appended claims.

Although the invention is applicable to the use of either a polyglycerol or a polyglycerol ester or a polyethylene glycol, or a polypropylene glycol, or a polymer of ethylene oxide and propylene oxide, or a polymer of ethylene oxide and 1-amino-2-hydroxyethanol, the most preferred substances for the purposes of the invention are the polyglycerols and the polyglycerol esters.

The use of the polyglycerols and polyglycerol esters for the purposes of the present invention provide numerous advantages. Aside from the advantages in effectivity, which will be further discussed below, one of the primary advantages of these compounds is that the body is able to utilize the polyglycerols and polyglycerol esters just like common fats and oils so that there is no accumulation or toxic effect whatsoever even upon extensive and high dosage use of these substances. As a matter of fact, these substances are so safe that the Food and Drug Administration has approved use of these substances in foods.

I have discovered, however, that these substances in addition to the safety which permits their use as and in foods, have marked effectiveness as osmotic agents to decrease intraocular and intracranial pressure which permits the use thereof in the treatment of glaucoma, preoperatively in cataract removal cases, etc.

Another advantage of the present invention is that it is possible by adjusting the degree of esterification of the polyglycerols to adjust the speed of the relief in the body so that it is possible to provide either quick acting compositions, slow acting compositions, or compositions which both act quickly and over a prolonged period of time.

While glycerin itself might have some suitability as an osmotic agent to reduce intraocular pressure, the compounds of the present invention provide several advantages, in addition to greater effectiveness, over glycerin. One of the advantages is that glycerin cannot be taken as freely as the polyglycerols and polyglycerol esters of the present invention, because prolonged and extensive administration of glycerin can cause gastric and other upsets. Furthermore, glycerin is highly unpalatable and is difficult to take in concentrated form. The polyglycerols and polyglycerol esters of the present invention, on the other hand, can easily be taken in concentrated form. In fact, those polyglycerols and polyglycerol esters can be taken in the form of capsules for the biscous liquid polyglycerols and polyglycerol esters, and in capsule or tablet form for the solid, powdered polyglycerols and polyglycerol esters.

Among the most suitable polyglycerols and polyglycerol esters for purposes of the present invention are:

Triglycerol
Hexaglycerol
Decaglycerol
Triglycerol monostearate
Triglycerol monooleate
Hexaglycerol monostearate
Hexaglycerol monooleate
Hexaglycerol dioleate
Hexaglycerol hexaoleate
Decaglycerol monostearate
Decaglycerol monooleate
Decaglycerol monolaurate
Decaglycerol tristearate
Decaglycerol trioleate
Decaglycerol trilinoleate
Decaglycerol decastearate
Decaglycerol decaoleate
Decaglycerol decalinoleate
Triglycerol mono shortening ("Drewpol 3–1–SH")
Hexaglycerol mono shortening ("Drewpol 6–1–SH")
Hexaglycerol di shortening ("Drewpol 6–2–SH")
Decaglycerol mono shortening ("Drewpol 10–1–SH")
Decaglycerol tri shortening ("Drewpol 10–3–SH")
Diglycerol
Tetraglycerol
Pentaglycerol
Hexaglycerol
Heptaglycerol
Octaglycerol
Monaglycerol
Pentaglycerol monostearate
Triglycerol mono cottonseed
Pentaglycerol mono cottonseed
Triglycerol mono hydrogenated cottonseed
Pentaglycerol mono hydrogenated cottonseed

The preferred glycerols and glycerol esters for the purpose of the present invention are triglycerol, decaglycerol, hexaglycerol, triglycerol monostearate, hexaglycerol distearate, decaglycerol tetraoleate, and decaglycerol tristearate. The most preferred substances are decaglycerol, decaglycerol monopalmitate and decaglycerol tetralinoleate.

It can be seen, however, from the above list, that the invention is applicable to all of the polyglycerols and particularly the polyglycerols from diglycerol to decaglycerol and partial and complete esters thereof with C_2 to C_{24} fatty acids which are either saturated, mono-unsaturated or poly-unsaturated.

The dosage of the polyglycerols and polyglycerol esters of the present invention to lower intraocular pressure will vary depending upon the molecular weight of the particular polyglycerol or polyglycerol esters as well as upon the number of hydroxyl groups thereof. A typical dosage is about 10 grams, three times a day. However, much lower dosages of as little as 1–2 grams, three times a day, and as high as 30–50 grams, three times a day, can be used. As mentioned above, the advantage of the polyglycerols and polyglycerol esters of the present invention is the complete lack of toxicity.

Although the invention is not meant to be limited as to any specific theory as to how any of the compounds which are used according to this invention achieve the desired effect, the following theory is given in the hope that it will help other investigators in this art and will aid in the research in this field. The invention is, of course, not limited to the theory.

It is believed that the polyglycerols act by means of distribution across membranes which results in an adjustment of osmotic pressures. The polyglycerols as well as the polyglycols of this invention are molecules of relatively large size and apparently cross membranes with less facility than do smaller molecules such as glycerol itself or the lower glycols. In addition, the polyglycerols and the higher polyglycols of the invention do not enter the triose-phosphate and other metabolic pathways as readily as glycerol and the lower glycols, and consequently, the compounds of the invention have a more effective therapeutic half life.

The lower glycols such as ethylene glycol and diethylene glycol are readily metabolized to or readily contribute to undesired concentrations of oxalate ions, and therefore, these substances have not found acceptance for human consumption. However, the triethylene glycol and higher ethylene glycols act similarly to the polyglycerols and can can be suitably used for the purposes of the present invention.

As a practical matter, the polyethylene glycols, and likewise the polypropylene glycols should not be used beyond a molecular weight of about 12,000. This higher molecular weight limitation is mainly a practical limitation because the higher polymers tend to become less and less water soluble or easily dispersible in physiological fluids.

The same comments apply with respect to the mixed polymers of propylene oxide and ethylene oxide and to the mixed polymers of ethylene oxide and 1-amino-2-hydroxyethanol.

The compounds of the invention are useful for the purposes of the invention whereas ordinary dietary proteins do not produce these beneficial effects. These ordinary dietary proteins include caseine and albumen, and the same are readily hydrolyzed to amino acids by proteolytic enzymes. On the other hand, the compounds of the invention are not metabolized readily by the body, they have a low antigenicity and are readily usable for the purposes of this invention.

DESCRIPTION OF PREFERRED EMBODIMENTS

The following examples are given to further illustrate the invention. The scope of the invention is not, however, meant to be limited to the specific details of these examples.

Example 1

Large gelatin capsules are filled with 5 grams each of decaglycerol. In the treatment of glaucoma, the capsules are administered as two capsules, three times a day. It is found that these capsules are wholly effective in reducing the intraocular pressure associated with glaucoma so as to relieve the glaucoma.

Example 2

Gelatin capsules are filled with 5 grams of decaglycerol monopalmitate. These capsules are administered as 2 capsules, three times a day, for the reduction of intraocular pressure.

Example 3

Large sized gelatin capsules are filled with 10 grams each of decaglycerol trilinoleate. These capsules are administered in the form of 1 to 2 capsules, three times a day, for the reduction of intraocular pressure.

Example 4

Large gelatin capsules are filled with 5 grams each of triethylene glycol. These capsules can be administered as two capsules, three times a day, for the treatment of glaucoma. The capsules are effective in reducing the intraocular pressure associated with glaucoma so as to relieve the glaucoma.

Example 5

Gelatin capsules are filled with 5 grams each of decapropylene glycol. These capsules are administered as capsules, three times a day, for the reduction of intraocular pressure.

Capsules are similarly filled with the reaction product of three molecules of ethylene oxide with three molecules of 1-amino-2-hydroxyethanol, and used in the same manner.

What is claimed is:

1. Method of reducing intraocular pressure, which comprises administering to a patient requiring reduction of intraocular pressure an effective amount of a substance selected from the group consisting of polyglycerols from diglycerol to decaglycerol, and fatty esters thereof with C_2 to C_{24} fatty acids.

2. Method according to claim 1 wherein said substance is decaglycerol.

3. Method according to claim 1 wherein said substance is decaglycerol monopalmitate.

4. Method according to claim 1 wherein said substance is decaglycerol trilinoleate.

5. Method according to claim 1 wherein said substance is administered orally in a daily dose of about 5–30 grams, one–three times per day.

6. Method according to claim 5 wherein said substance is decaglycerol tetralinoleate.

7. Method according to claim 1 wherein said substance is decaglycerol tetralinoleate.

References Cited

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