The most preferable polyol component b) is a polycarbonate polyol or a mixture of a polycarbonate polyol with a polyether and/or polyester polyol.

A preferable chain extender c) is a mixture of a straight chain oligomer, prepared from 1,6-hexanediol and ε-caprolactone, and hydroquinone bis(2-hydroxyethyl)-ether. Another preferable chain extender c) is selected from long chain aliphatic diols with more than 10 carbon atoms, such as 1,10-decanediol or 1,12-dodecanediol.

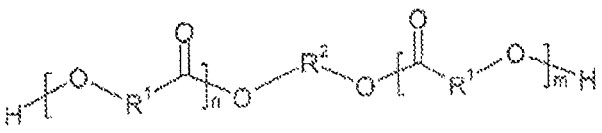
Another object of the present invention is to provide an intrauterine system, which is easy to insert and remove without causing any pain, is easy and comfortable to use and has a shape and size fitting to the size of the endometrial cavity thus minimizing or eliminating the possibility of expulsion and avoiding side effects, for example such as caused by the irritation of the endometrium.

A further object of the invention is an intra-uterine system, which has a safe and optimized design to avoid the perforations or penetrations of the uterine wall.

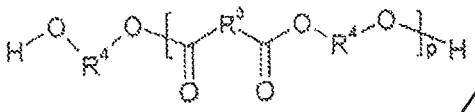
~~Still another object of the invention is a convenient and reliable method for delivering~~ therapeutically active substances to a female mammal. The method involves the steps of preparing an intrauterine system having a continuous, closed and flexible frame of polygonal shape and a reservoir connected to the frame, wherein the frame comprises a thermoplastic polyurethane elastomer and the reservoir comprises at least one core comprising a polymer composition and a therapeutically active substance mixed therein, positioning and maintaining the intrauterine system in the uterus of the female mammal to be treated, and maintaining it there for a prolonged period of time, or at least for a time sufficient to deliver an effective amount of the substance to the female mammal.

A further object of the invention is a light-stable, thermoplastic polyurethane elastomer for intra-uterine systems with improved blooming behaviour and very good hydrolytic stability comprising the reaction product of a polycarbonate polyol or a mixture of a polycarbonate polyol with a polyether polyol and/or a polyester polyol, 1,6-hexamethylenediisocyanate and optionally additional (cyclo)aliphatic diisocyanates and at least one difunctional chain extender c1) with a number average molecular weight Mn of from 60 to 286 and optionally ~~at least one chain extender c2) with a number average molecular weight Mn between 104~~

~~and 500 g/mol, which is different from the chain extender c1), corresponding to formula (I)~~ or formula (II).



(I)



(II)

in which

R^1 represents a branched or unbranched alkylene radical with from 1 to 12 C atoms or a substituted or unsubstituted alkarylene radical with from 6 to 24 C atoms,

R^2, R^4 each represents a branched or unbranched alkylene radical with from 1 to 12 C atoms or an alkoxyalkylene radical with from 1 to 12 C atoms or a substituted or unsubstituted alkarylene radical with from 6 to 24 C atoms or a substituted or unsubstituted alkoxyarylene radical with from 6 to 24 C atoms,

R^3 represents a branched or unbranched alkylene radical with from 1 to 8 C atoms or a substituted or unsubstituted alkarylene radical with from 6 to 20 C atoms or a substituted or unsubstituted arylene radical with from 6 to 20 C atoms or a substituted or unsubstituted aralkylene radical with from 6 to 20 C atoms,

n, m each represent 0 to 10, where $n + m \geq 1$, and

p ~~represents 1 to 10.~~

purpose. Such catalysts particularly include organic and inorganic acid salts of, and organometallic derivatives of bismuth, tin, iron, antimony, cobalt, thorium, aluminum, zinc, nickel, cerium, molybdenum, vanadium, copper, manganese and zirconium, as well as phosphines and tertiary organic amines. Representative catalysts include for example sterically hindered bismuth catalysts, for example such as bismuth-neodecanoate, bismuth-octoate or bismuth carboxylate (BiCat), tin compounds such as stannous diacetate, stannous dioctoate, stannous dilaurate, or the dialkyltin salts of aliphatic carboxylic acids, e.g. dibutyltin diacetate, dibutyltin dilaurate, dibutyltin dioctoate, titanic esters, iron compounds, e.g. ferric acetylacetonate or the like. The amounts of the catalysts usually used are from 0.0001 to 0.5 part by weight per 100 parts by weight of polyhydroxy compound (b).

Besides catalysts, conventional auxiliaries may also be added to the structural components, including for example surface-active substances, flame retardants, nucleating agents, anti-oxidants, coatings, coloring materials, preservatives, lubricants, and mold-release agents, dyes, and pigments, and, if appropriate, stabilizers, e.g. with respect to hydrolysis, light, heat, or discoloration, inorganic and/or organic fillers, material, which can for example be used for identification or detection of the intrauterine system, such as metallic or magnetic particles or an X-ray contrast medium like barium sulphate, reinforcing agents, and plasticizers.

Examples of suitable UV light stabilizers which may be used include by way of non-limiting example Tinuvin® 144, Tinuvin® 234, Tinuvin® 328, Tinuvin® 765, Tinuvin® 770, all of which are commercially available. Among the commercially available anti-oxidants which are considered useful are UVINUL® A03 and IRGANOX® 1010, IRGANOX® 1035, IRGANOX® 1076, IRGANOX® 1098 and IRGANOX® 1222. A suitable commercially available anti-oxidant and metal deactivator is IRGANOX® MD 1024.

The polyurethane elastomer ~~of the present invention~~ can be prepared by reacting a polycarbonate diol with a diisocyanate compound and chain extenders in the presence of a catalyst and optionally fillers and optionally in the presence of an antioxidant and/or a curing agent and other additives, if the case requires. In addition a suitable lubricant or a mold release agent can be used. A known method selected from a one-shot method, a prepolymer method, etc. can be employed.

According to a preferred embodiment, the thermoplastic polyurethane elastomer is made by reacting a polycarbonate diol, prepared from 1,6-hexanediol and dimethyl carbonate and having a number average molecular weight of from 501 to 3000 g/mol, preferably of from 501 to 2500 g/mol and more preferably of from 1000 to 2500, with 1,6-hexamethylenediisocyanate, a mixture of a straight chain oligomer, prepared from 1,6-hexanediol and ε-caprolactone, and hydroquinone bis(2-hydroxyethyl)ether as chain extender. Another preferred thermoplastic polyurethane elastomer is made by reacting a polycarbonate diol, prepared from 1,6-hexanediol and dimethylcarbonate and having number average molecular weights of from 501 to 3000 g/mol, preferably of from 501 to 2500 and more preferably of from 1000 to 2500 g/mol with 1,6-hexamethylenediisocyanate and 1,12-dodecanediol as chain extender.

In ~~O~~one embodiment of the invention the~~therefore is a~~ light-stable, thermoplastic polyurethane elastomer comprises~~ing~~ the reaction product of

a) one or more aliphatic and/or cycloaliphatic diisocyanate with an isocyanate content of 32 to 75 weight-%,

b) at least one polyol component having a number-average molecular weight Mn of from 501 to 10.000 g/mol and on average from 1.8 to not more than 3.0 Zerewitinoff-active hydrogen atoms,

c) at least one low molecular weight polyfunctional alcohol component having a number-average molecular weight Mn of from 60 to 500 g/mol and on average from at least 1.8 to not more than 3.0 Zerewitinoff-active hydrogen atoms as chain extender,

d) optionally monofunctional alcohols as chain terminators,

in the presence of

e) one or more catalysts,

with the addition of

18. An intrauterine system according to any of claims 1-17, characterized in that said system comprises at least one image enhancing means for improving the detection and/or location of the of the system.

19. An intrauterine system according to any of claims 1-18, characterized in that the frame or the reservoir comprises retention or locking means to retain the reservoir and to prevent it from sliding off.

20. A method for manufacturing an intrauterine system according to one of the preceding claims having a closed continuous and flexible frame of polygonal shape and a reservoir comprising at least one therapeutically active substance, which reservoir is connected to the inner surface of the frame, wherein the frame comprises a thermoplastic polyurethane elastomer, said method comprising injection molding, extruding or compressing the frame and the reservoir by using a sequential process comprising the steps of preparing the frame, preparing the first composition comprising a therapeutically active substance and a polymer composition to provide a core, preparing the second composition comprising a polymer composition to provide a membrane encasing the core, combining the core and the membrane to produce a reservoir, and connecting together the reservoir and the frame.

~~21. A light-stable, thermoplastic polyurethane elastomer comprising the reaction product~~ of

~~a) an isocyanate component comprising:~~

a1) from 65 to 100 mol-% of 1,6-hexamethylene diisocyanate and

a2) from 0 to 35 mol-% of an aliphatic diisocyanate other than 1,6-hexamethylene diisocyanate or a mixture of aliphatic and/or cycloaliphate diisocyanates which does not include 1,6-hexamethylene diisocyanate,

b) a polyol component comprising:

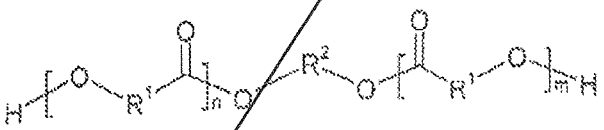
b1) from 65 to 100 mol-% of at least one polycarbonate diol with a number average molecular weight of from 501 to 3000 g/mol and,

b2) from 0 to 35 mol-% of a polyether diol and/or a polyester diol with a number average molecular weight of from 501 to 4000 g/mol,

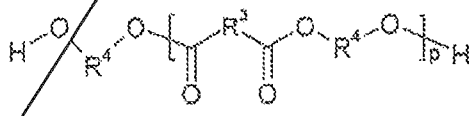
c) a chain extender component comprising:

c1) from 35 to 100 mol-% of at least one difunctional chain extender having a number average molecular weight of from 118 to 286 g/mol and

c2) from 0 to 65 mol-% of a chain extender with a number average molecular weight between 104 and 500 g/mol, which is different from the chain extender c1), corresponding to the formula (I) or formula (II)



(I)



(II)

in which

R^1 represents a branched or unbranched alkylene radical with from 1 to 12 C atoms or a substituted or unsubstituted alkarylene radical with from 6 to 24 C atoms,

R^2, R^4 each represents a branched or unbranched alkylene radical with from 1 to 12 C atoms or an alkoxyalkylene radical with from 1 to 12 C atoms or a substituted or unsubstituted alkarylene radical with from 6 to 24 C atoms or a substi-

~~tuted or unsubstituted alkoxyarylene radical with from 6 to~~ 24 C atoms,

R^3 represents a branched or unbranched alkylene radical with from 1 to 8 C atoms or a substituted or unsubstituted alkarylene radical with from 6 to 20 C atoms or a substituted or unsubstituted arylene radical with from 6 to 20 C atoms or a substituted or unsubstituted aralkylene radical with from 6 to 20 C atoms,

n, m each represent 0 to 10, where $n + m \geq 1$, and

p represents 1 to 10,

d) optionally monofunctional alcohols as chain terminators,

in the presence of

e) one or more catalysts,

with the addition of

f) from 0.1 to 35 wt.-%, based on the weight of the thermoplastic polyurethane made of components a) to d), of inorganic fillers,

g) optionally, further additives and/or auxiliary substances

in which the ratio of the isocyanate groups of a) to isocyanate-reactive groups of b), c) and d) is from 0.9:1 to 1.1:1.