The invention relates both to infusion solutions, which are ready for use, of 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-quinoline-3-carboxylic acid (= ciprofloxacin, to be designated active compound in the text which follows) and to other presentations, which, before administration, are converted into infusion solutions of this type. The invention likewise relates to the process for the preparation of the infusion solutions.

Solutions of lactic acid salts of piperazinyl-quinoline- and piperazinyl-azaquinolinecarboxylic acids are described in European Patent Application EP-A-138,018.

European Patent Application EP-A-49,355 relates to 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-quinoline-3-carboxylic acid and its pharmaceutically utilizable salts.

In Antimicrobial Agents and Chemotherapy 27,375 (1985) aqueous ciprofloxacin solutions are described by Gert Höffken et al. It should be noted in this connection that it is not possible to prepare a solution of 50 mg or 100 mg of ciprofloxacin lactate having a molar ratio of ciprofloxacin/lactic acid equal to 1 in 50 ml of 0.9 % NaCl solution. The active compound does not dissolve in preparations of this type.

The present invention relates to infusion solutions of 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-quinoline-3-carboxylic acid (= ciprofloxacin) containing 0.015 to 0.5 g of the active compound per 100 ml of aqueous solution and, depending on the active compound concentration, 1.04 to 2.20 mol, relative to 1 mol of active compound, of one or more physiologically tolerated acids, and where when several acids are present their total content does not exceed the amount of 2.20 mol, relative to 1 mol of active compound.

In addition to the active compound, water and other customary formulating auxiliaries, the infusion solutions according to the invention preferably contain an amount, which suffices to dissolve the active compound

and to stabilize the solution, of one or more acid(s) from the group comprising hydrochloric acid, methanesulphonic acid, propionic acid, succinic acid, glutaric acid, citric acid, fumaric acid, maleic acid, tartaric acid, glutamic acid, gluconic acid, glucuronic acid, galacturonic acid, ascorbic acid, phosphoric acid, adipic acid, hydroxyacetic acid, sulphuric acid, nitric acid, acetic acid, malic acid, L-aspartic acid and lactic acid.

Lactic acid and hydrochloric acid or mixtures of hydrochloric acid and lactic acid are particularly preferred.

Furthermore preferred are infusion solutions which contain 0.015 to 0.5 g of the active compound per 100 ml of aqueous solution and, depending on the active compound concentration, up to 5.0 mol, in particular 0.9 to 5.0 mol, and particularly preferably 1.04 to 2.20 mol, relative to 1 mol of active compound, of one or more physiologically tolerated acids, and where several acids are present their total content does not exceed the amount of 5.0 mol, relative to 1 mol of active compound.

Moreover, the invention preferably relates to infusion solutions which contain 0.015 to 0.5 g of the active compound per 100 ml of aqueous solution and 1.04 to 1.40 mol, relative to 1 mol of active compound, of lactic acid. Infusion solutions of the active compound which contain 1.12 to 1.24 mol, relative to 1 mol of active compound, of lactic acid are particularly advantageous.

The infusion solutions according to the invention can also be modified in such a way that they contain up to 0.5 g of the active compound per 100 ml of aqueous solution and up to 1 mol, relative to 1 mol of active compound, of lactic acid and another physiologically tolerated acid, with the proviso that the total amount of acid is, depending on the active compound concentration, more than 1.04 mol but does not exceed 2.2 mol, relative to 1 mol of active compound.

The minimum amount of acid necessary per mol of active compound for the dissolution depends on the active

compound concentration and the acid(s) used, and thus is not constant. However, within the limits according to the invention it can be determined by simple experiments. Furthermore, it should be noted that the data in the amounts of acid relate only to the amounts which, according to generally known chemical laws, are not converted by the addition of bases into the corresponding salt(s). Dissociation of the acids was left out of account in the data on the amounts so that they relate to the amount of dissociated and undissociated acid.

The lactic acid used in the formulations has a content of less than 25% (w/w), specifically for reasons of processing technology. The use of concentrated lactic acid - for example a 90% strength (w/w) product - gives rise to difficulties when the pH of the formulations according to the invention is to be adjusted after addition of the lactic acid - for example with hydrochloric acid or sodium hydroxide solution - with the objective that the adjusted pH remains constant, or changes only inconsiderably, during the remainder of the preparation process (such as, for example, a heat treatment at about 120°C for about 20 min) and/or during storage.

The infusion solutions according to the invention can also contain other formulating aids such as thickeners, resorbents, light protection agents, absorption inhibitors, crystallization accelerators, absorption accelerators, crystallization retardants, complexing agents, antioxidants, isotonicizing agents and/or euhydrogenating agents.

The osmolality of the infusion solutions is 0.20 to 0.70 Osm/kg, preferably 0.26 to 0.39 Osm/kg and is adjusted by isotonicizing agents such as NaCl, sorbitol, mannitol, glucose, sucrose, xylitol, fructose and glycerol or mixtures of such substances. Where appropriate, it is also possible to use for this substances which are contained in conventional commercially available infusion vehicle solutions.

The customary infusion vehicle solutions include

perfectly possible.

The infusion solutions according to the invention can be in the form of dosage units, suitable for infusion, with removable contents of 40 to 600 ml, preferably 50 to 120 ml.

However, the invention also relates to lyophilizates which have been prepared by customary techniques and which are converted into the infusion solutions according to the invention by dissolution in solvents suitable for this purpose - such as, for example, conventional infusion vehicle solutions. Lyophilizates of this type can be obtained by freeze-drying of various starting solutions such as, for example, the infusion solutions according to the invention. It is likewise possible to freeze-dry considerably more dilute solutions as well as considerably more concentrated solutions than the infusion solutions according to the invention.

The lyophilizates can be prepared both by freeze-drying in the final container such as, for example, in a bottle or ampoule made of glass or plastic, and by bulk freeze-drying combined with dispensing the lyophilizate into a container suitable for this purpose, which takes place at a later time.

The dissolution of the lyophilizate before the administration can be brought about both by addition of a solution, which is suitable for this purpose, into the container containing the lyophilizate and by addition of the lyophilizate to a suitable solution, or by a combination of procedures of these types.

The composition of the lyophilizates can likewise vary very widely, depending on the composition of the solution which is used for the dissolution.

It can vary from pure active compound to a lyophilizate which contains all the constituents which are to be administered, apart from water.

The invention likewise relates to combinations of lyophilizates with solutions containing active compound, which are converted into the infusion solutions according to the invention before administration.

The invention also includes concentrates and suspensions which are converted into the solutions according to the invention before administration.

It is possible in this context for these concentrates and suspensions to have various compositions. One possibility would be that which requires merely the addition of water for dilution or dissolution in order to prepare the infusion solutions according to the invention.

This invention relates to all combinations of concentrates and/or suspensions and to solutions which are necessary for dilution or dissolution and which result in the solutions according to the invention.

The invention also relates to other presentations or combinations of presentations which finally result in the infusion solutions according to the invention - and this irrespective of the procedure.

The containers into which lyophilizates, concentrates and other presentations, such as, for example, suspensions, are dispensed can consist both of glass and of plastic. In this connection, the container materials can contain substances which confer a particular protection on the contents, such as, for example, a protection from light or a protection from oxygen.

The present invention additionally relates to a process for the preparation of infusion solutions, containing 0.015 to 0.5 % by weight of 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-quinoline-3-carboxylic acid (= ciprofloxacin). This process comprises mixing a suitable amount of the active compound, where appropriate in the form of a salt, such as an alkali metal or alkaline earth metal salt or addition salt, of a hydrate or of a hydrate of the salt, or in the form of mixtures of these salts or hydrates, with the amount of a physiologically tolerated acid or of a mixture of several physiologically tolerated acids which, in relation to the amount which just suffices to dissolve the active compound or its salts or hydrates, represents an excess preventing separation out of the active compound,

adding, where appropriate, formulating auxiliaries, and filling up with water or a customary infusion vehicle solution in such a manner that the concentration of the active compound is adjusted to the range from 0.015 to 0.5 g. In this connection, it has to be remembered that when the alkali metal or alkaline earth metal salts of the active compound are used the amounts of acid which are mentioned above as being necessary for the dissolution contain the amount which is needed to neutralize the active compound anion, and that when addition salts are used a part of the amounts of acid which are necessary is already contained in the active compound salt to be used.

Furthermore, care has to be taken in the preparation that the solution complies with the properties relating to pH, amounts of acid and osmolalities which have already been detailed.

In the case where the active compound is used in the salt form, it is possible and expedient to use an acid whose anion corresponds to the anion of the active compound salt or salt hydrate.

Where appropriate, the active compound is suspended in water, and up to 5 mol, relative to 1 mol of active compound, of lactic acid are added, and then, where appropriate, another physiologically tolerated acid or a mixture of such acids, in particular hydrochloric acid, is added, with the proviso that the total amount of acid does not exceed 5.0 mol, relative to 1 mol of active compound, but does exceed 0.9 mol, relative to 1 mol of active compound, and then, where appropriate, further formulating auxiliaries are added, in particular NaCl, which is also, where appropriate, produced by a neutralization reaction in the formulation mixture, and the desired active compound concentration is adjusted by making up with water.

The pH of the infusion solutions according to the invention can be adjusted with (physiologically) tolerated acids and/or bases to the abovementioned values, that is to say 3.0 to 5.2, in particular 3.6 to 4.7.

To speed up the preparation process, in particular the dissolution of solid components, it is possible gently to heat the solutions, or only a part thereof, preferably to temperatures between 20°C and 80°C.

It has been possible particularly economically to prepare the solutions according to the invention via concentrated solutions. For this purpose, the amount of active compound necessary for a batch was dissolved with the major amount of acid necessary for the complete batch (for example >95% relative to the molar basis) in a little water - where appropriate with heating. This concentrate was then subsequently diluted. After dilution, any other auxiliaries - such as, for example, sodium chloride for isotonicizing - were added, as were the amounts of acid which were still lacking, where appropriate.

The infusion solutions according to the invention are used for the therapeutic treatment of the human or animal body.

The infusion solutions according to the invention have a low toxicity and a broad spectrum of antibacterial activity against Gram-positive and Gram-negative microbes, in particular against Enterobacteriaceae; especially including those which are resistant to various antibiotics such as, for example, penicillins, cephalosporins, aminoglycosides, sulphonamides and tetracyclines.

These valuable properties make it possible to use them in medicine.

The infusion solutions according to the invention are active against a very broad spectrum of microorganisms. They can be used to combat Gram-negative and Gram-positive bacteria and bacteria-like microorganisms and to prevent, ameliorate and/or heal illnesses caused by these pathogens.

The infusion solutions according to the invention are particularly active against bacteria and bacteria-like microorganisms. They are therefore particularly

suitable for the prophylaxis and chemotherapy of local and systemic infections, caused by these pathogens, in human medicine and veterinary medicine.

For example, local and/or systemic illnesses caused by the following pathogens or by mixtures of the following pathogens can be treated and/or prevented:

Gram-positive cocci, for example Staphylococci (Staph. aureus, Staph. epidermidis) and Streptococci (Strept. agalactiae, Strept. faecalis, Strept. pneumoniae, Strept. pyogenes); Gram-negative cocci (Neisseria gonorrhoeae) and Gram-negative rods such as Enterobacteriaceae, for example Escherichia coli, Hämophilus influenzae, Citrobacter (Citrob. freundii, Citrob. divernis), Salmonella and Shigella; furthermore Klebsiella (Klebs. pneumoniae, Klebs. oxytoca), Enterobacter (Ent. aerogenes, Ent. agglomerans), Hafnia, Serratia (Serr. marcescens), Proteus (Pr. mirabilis, Pr. rettgeri, Pr. vulgaris), Providencia, Yersinia, and the genus Acinetobacter. Furthermore, the antibacterial spectrum covers the genus Pseudomonas (Ps. aeruginosa, Ps. maltophilia) and strictly anaerobic bacteria such as, for example, Bacteroides fragilis, representatives of the genus Peptococcus, Peptostreptococcus and the genus Clostridium; furthermore Mycoplasmas (M. pneumoniae, M. hominis, M. urealyticum) as well as Mycobacteria, for example Mycobacterium tuberculosis.

The above list of pathogens is purely illustrative and is in no way to be interpreted as restrictive. The following may be mentioned as examples of illnesses which may be cuased by the said pathogens or combined infections and which can be prevented, ameliorated or healed by the compounds according to the invention:

Infectious illnesses in humans such as, for example, otitis, pharyngitis, pneumonia, peritonitis, pyelonephritis, cystitis, endocarditis, systemic infections, bronchitis (acute and chronic), septic infections, illnesses of the upper airways, diffuse panbronchiolitis, pulmonary emphysema, dysentery, enteritis, liver abscesses, urethritis, prostatitis, epididymitis,

gastrointestinal infections, bone and joint infections, cystic fibrosis, skin infections, postoperative wound infections, abscesses, phlegmon, wound infections, infected burns, burns, infections in the mouth, infections after dental operations, osteomyelitis, septic arthritis, cholecystitis, peritonitis with appendicitis, cholangitis, intraabdominal abscesses, pancreatitis, sinusitis, mastoiditis, mastitis, tonsillitis, typhoid, meningitis and infections of the nervous system, salpingitis, endometritis, genital infections, pelveoperitonitis and eye infections.

Apart from humans, it is also possible to treat bacterial infections in other species. The following may be mentioned as examples:

Pig: coli diarrhoea, enterotoxaemia, sepsis, dysentery, salmonellosis, metritis-mastitis-agalactiae syndrome, mastitis;

ruminants (cattle, sheep, goat): diarrhoea, sepsis, bronchopneumonia, salmonellosis, pasteurellosis, mycoplasmosis, genital infections;

horse: bronchopneumonias, joint ill, puerperal and postpuerperal infections, salmonellosis;

dog and cat: bronchopneumonia, diarrhoea, dermatitis, otitis, urinary tract infections, prostatitis;

poultry (chicken, turkey, quail, pigeon, ornamental birds and others): mycoplasmosis, E. coli infections, chronic respiratory tract illnesses, salmonellosis, pasteurellosis, psittacosis.

It is likewise possible to treat bacterial illnesses in the rearing and maintenance of productive and ornamental fishes, the antibacterial spectrum extending beyond the pathogens mentioned above to further pathogens such as, for example, Pasteurella, Brucella, Campylobacter, Listeria, Erysipelothrix, Corynebacteria, Borellia, Treponema, Nocardia, Rickettsia and Yersinia.

Examples

The molar ratio - abbreviated to R - stated in the examples which follow always relates to the substance which is mentioned first in the relevant example.

Examp. No.	Formulation		Micromole	R
1	Ciprofloxacin	90 mg	272	1.00
	Lactic acid 20% (w/w)	144.3 mg	320	1.18
	Hydrochloric acid	1.5 mg	48	0.15
	Sodium chloride	5.4 g	-	-
	Water	ad 600.0 ml	-	-
		pH: approx. 4.3		
		Osm: approx. 0.29 Osm/kg		
2	Ciprofloxacin	150 mg	453	1.00
	Lactic acid 10% (w/w)	558 mg	658	1.37
	Hydrochloric acid	7.8 mg	214	0.47
	Glucose	30.0 g	-	-
	Water	ad 600.0 ml	-	-
		pH: approx. 3.7		
		Osm: approx. 0.29 Osm/kg		

Examp. No.	Formulation			Micromole	R
3	Ciprofloxacin acetate		118 mg	302	1.00 (containing an equimolar amount of acetic acid)
	Acetic acid		3.6 mg	60	0.20
	Lactic acid 10% (w/w)		272 mg	302	1.00
	Sorbitol		10.0 g	-	-
	Water	ad	200.0 ml		
		pH:	4.7		
		Osm:	0.30 Osm/kg		
4	Ciprofloxacin		200 mg	604	1.00
	Propionic acid		54 mg	724	1.20
	Lactic acid 20% (w/w)		136 mg	604	1.00
	Glucose		20.0 g		
	Water	ad	400.0 ml		
		pH:	4.7		
		Osm:	0.3 Osm/kg		

Examp. No.	Formulation			Micromole R	
5	Ciprofloxacin		200 mg	604	1.00
	Lactic acid 1% (w/w)		7440 mg	826	1.37
	1 N hydrochloric acid		0.285 ml	285	0.47
	Mannitol		6.2 g	-	-
	Water	ad	200 ml		
		pH:	3.7		
		Osm:	0.37 Osm/kg		

Examp. No.	Formulation			Micromole	R
6	Ciprofloxacin		50 mg	151	1.00
	Lactic acid 10% (w/w)		160 mg	178	1.18
	Sodium chloride		625 mg		
	Water	ad	50 ml		
		pH:	4.4		
		Osm:	0.40 Osm/kg		

Examp. No.	Formulation	mg	Micromole	R
7	Ciprofloxacin	500 mg	1509	1.00
	Lactic acid 2% (w/w)	6727 mg	1494	0.99
	Sorbitol	25.0 g		
	Water	ad 500 ml		
		pH: 5.0		
		Osm: 0.29 Osm/kg		
8	Ciprofloxacin lactate	127 mg	302	1.00 (containing an equimolar amount of lactic acid)
	Maleic acid	42 mg	364	1.20
	Mannitol	5.0 g		
	Water	ad 100.0 ml		
		pH: 3.1		
		Osm: 0.30 Osm/kg		

Examp. No.	Formulation			Micromole	R
9	Ciprofloxacin		200 mg	604	1.00
	Lactic acid 20% (w/w)		297 mg	659	1.09
	Glutaric acid		40 mg	302	0.50
	Fructose		10.0 g		
	Water	ad	200 ml		
		pH:	4.3		
		Osm:	0.30 Osm/kg		
10	Ciprofloxacin		200 mg	604	1.00
	Lactic acid 10% (w/w)		566 mg	628	1.04
	Sodium chloride		0.9 g	-	-
	Water	ad	100.0 ml	-	-
		pH:	4.9		
		Osm:	0.29 Osm/kg		
11	Ciprofloxacin		400 mg	1207	1.00
	Lactic acid 20% (w/w)		745 mg	1654	1.37
	Hydrochloric acid		20.8 mg	570	0.47
	Sodium chloride		1800 mg		
	Water	ad	200 ml		
		pH:	3.7		
		Osm:	0.29 Osm/kg		

Examp. No.	Formulation			Micromole	R
12	Ciprofloxacin . 5 H_2O		509 mg	1207	1.00
	Lactic acid 5% (w/w)		2568 mg	1425	1.18
	Hydrochloric acid		6.6 mg	180	0.15
	Glucose		5.0 g	-	-
	Water	ad	200 ml	—	—
		pH:	4.2		
		Osm:	0.30 Osm/kg		

Examp. No.	Formulation			Micromole	R
13	Ciprofloxacin		100 mg	302	1.00
	Lactic acid 0.4% (w/w)		7407 mg	329	1.09
	1 M hydrochloric acid		3.42 ml	3420	11.32
	2 M sodium hydroxide solution		1.71 ml	3420	11.32
	Sodium chloride		0.25 g		
	Water	ad	50.0 ml		
		pH:	4.7		
		Osm:	Osm/kg		

Examp. No.	Formulation			Micromole R	
14	Ciprofloxacin HCl . H_2O		232 mg	604	1.00 (containing an equimolar amount of hydrochloric acid)
	Lactic acid 5% (w/w)		1288 mg	715	1.18
	2 M sodium hydroxide solution		0.257 ml	514	0.85
	Sodium chloride		0.873 g		
	Water	ad	100 ml		
		pH:	4.2		
		Osm:	0.30 Osm/kg		

Examp. No.	Formulation			Micromole	R
15	Ciprofloxacin Na (Sodium salt of ciprofloxacin)		213 mg	604	1.00
	Lactic acid 10% (w/w)		744 mg	826	1.37
	Hydrochloric acid		32.4 mg	888	1.47
	Glucose		4.8 g		
	Water	ad	100.0 ml		
		pH:	3.7		
		Osm:	0.30 Osm/kg		
16	Calcium salt of ciprofloxacin		212 mg	604	1.00
	Lactic acid 2% (w/w)		3220 mg	715	1.18
	Hydrochloric acid		25.3 mg	693	1.15
	Glycerol		2.6 g	-	-
	Water	ad	500.0 ml		
		pH:	4.3		
		Osm:	0.30 Osm/kg		

Examp. No.	Formulation			Micromole	R
17	Potassium salt of ciprofloxacin		233 mg	604	1.00
	Lactic acid 20% (w/w)		277 mg	615	1.018
	0.1 M hydrochloric acid		8.86 ml	886	1.47
	Glucose		5.0 g		
	Water	ad	100.0 ml		
		pH:	4.6		
		Osm:	0.30 Osm/kg		

Examp. No.	Formulation			Micromole	R
18	Ciprofloxacin gluconate		159 mg	302	1.00 (containing an equimolar amount of gluconic acid)
	Gluconic acid		12 mg	62	0.20
	Lactic acid 5% (w/w)		544 mg	302	1.00
	Glycerol		1.3 g	-	-
	Water	ad	50.0 ml		
		pH:	4.0		
		Osm:	0.30 Osm/kg		
19	Ciprofloxacin		500 mg	1509	1.00
	Galacturonic acid		351 mg	1811	1.20
	Sorbitol		25.0 g		
	Water	ad	250.0 ml		
		pH:	4.6		
		Osm:	0.3 Osm/kg		
20	Ciprofloxacin. 5 H_2O		127 mg	302	1.00
	Ascorbic acid		41 mg	366	1.21
	Glucose		2.5 g		
	Water	ad	50 ml		
		pH:	4.5		
		Osm:	0.30 Osm/kg		

Examp. No.	Formulation			Micromole R	
21	Ciprofloxacin lactate		509 mg	1207	1.00 (containing an equimolar amount of lactic acid)
	Hydroxyacetic acid		110 mg	1448	1.20
	Sodium chloride		1.8 g		
	Water	ad	200 ml		
		pH:	4.0		
		Osm:	0.30 Osm/kg		

Examp. No.	Formulation			Micromole	R
22	Ciprofloxacin		100 mg	302	1.00
	L. aspartic acid		78 mg	361	1.20
	Fructose		2.5 g		
	Water	ad	50.0 ml		
		pH:	4.5		
		Osm:	0.30 Osm/kg		
23	Ciprofloxacin		100 mg	302	1.00
	Lactic acid 20% (w/w)		204 mg	453	1.50
	0.1 M hydrochloric acid		2.11 ml	211	0.70
	Sorbitol		2.5 g		
	Water	ad	50.0 ml		
		pH:	3.3		
		Osm:	0.30 Osm/kg		

Examp. No.	Formulation			Micromole	R
24	Ciprofloxacin		200 mg	604	1.00
	Lactic acid 15% (w/w)		496 mg	826	1.37
	0.2 M hydrochloric acid		1.42 ml	284	0.47
	Glucose		5.00 g	-	-
	Water	ad	40.0 ml		
		pH:	3.7		
		Osm:	0.33 Osm/kg		
25	Ciprofloxacin lactate . 2 H_2O		3858 mg	7544	1.00 (containing an equimolar amount of lactic acid)
	Sodium chloride		4.5 g	-	-
	1 M hydrochloric acid		0.754 ml	754	0.10
	Water	ad	500ml		
		pH:	4.7		
		Osm:	0.30 Osm/kg		
26	Ciprofloxacin		500 mg	1509	1.00
	Lactic acid 1%		14814 mg	1645	1.09
	Sodium chloride		0.45 g		
	Water	ad	100.0 ml		
		pH:	4.7		
		Osm:	0.31 Osm/kg		

Examp. No.	Formulation			Micromole	R
27	Ciprofloxacin lactate . 2 H_2O		359 mg	754	1.00 (containing an equimolar amount of lactic acid)
	Lactic acid 20% (w/w)		2.6 mg	69	0.09
	Succinic acid		45 mg	381	0.51
	Sorbitol		2.5 g		
	Water	ad	50.0 ml		
		pH:	4.2		
		Osm:	0.32 Osm/kg		
28	Ciprofloxacin		500 mg	1509	1.00
	Lactic acid 10% (w/w)		1481 mg	1644	1.09
	Citric acid		159 mg	757	0.50
	Glucose		5.0 g		
	Water	ad	100.0 ml		
		pH:	3.8		
		Osm:	0.33 Osm/kg		

Examp. No.	Formulation			Micromole	R
29	Ciprofloxacin lactate		127 mg	302	1.00 (containing an equimolar amount of lactic acid)
	Ciprofloxacin fumarate		68 mg	151	0.50 containing an equimolar amount of fumaric acid
	Ciprofloxacin		50 mg	151	0.50
	Lactic acid 20%		160 mg	356	1.18
	Fructose		2.0 g		
	Water	ad	40.0 ml		
		pH:	3.9		
		Osm:	0.32 Osm/kg		

Examp. No.	Formulation			Micromole	R
30	Ciprofloxacin		500 mg	1509	1.00
	Lactic acid 25%		641 mg	1780	1.18
	Sodium chloride		0.9 g		
	Water	ad	100.0 ml		
		pH:	4.5		
		Osm:	0.30 Osm/kg		

Examp. No.	Formulation			Micromole R	
31	<u>Solution A</u>				
	Ciprofloxacin		100 mg	302	1.00
	Lactic acid 6% (w/w)		537 mg	358	1.19
	0.1 M hydrochloric acid		0.45 ml	45	0.15
	Sodium chloride		0.45 g		
	Water	ad	50.0 ml		
	<u>Solution B</u>				
	Glucose		12.5 g		
	Water	ad	250 ml		
	Prepare the solution ready for use by mixing solution A and B				

Examp. No.	Formulation			Micromole	R
32	Solution A				
	Ciprofloxacin		100 mg	302	1.00
	Lactic acid 2% (w/w)		1610 mg	358	1.19
	Hydrochloric acid		1.6 mg	45	
	Glucose		2.5 g		
	Water	ad	50 ml		
	Solution B				
	Sodium chloride		900 mg		
	Water	ad	100 ml		
	Prepare the solution ready for use by mixing solution A and B				

Examp. No.	Formulation			Micromole R	
33	**Solution A**				
	Ciprofloxacin lactate . 2 H_2O		276 mg	604	1.00 (containing an equimolar amount of lactic acid)
	Lactic acid 0.1% (w/w)		10.0 g	111	0.18
	Hydrochloric acid		3.3 mg	90	0.15
	Xylitol		4.2 g		
	Water	ad	100.0 ml		
	Solution B				
	Fructose		10.0 g		
	Water	ad	100.0 ml		
	Prepare the solution ready for use by mixing solution A and B				
34	**Solution A**				
	Ciprofloxacin		200 mg	604	1.00
	Lactic acid 10% (w/w)		644 mg	715	1.18
	0.1 M hydrochloric acid		0.90 ml	90	0.15
	Sodium chloride		0.9 g		
	Water	ad	100.0 ml		
	Solution B				
	Xylitol		12.5 g		
	Water	ad	250 ml		
	Prepare the solution ready for use by mixing solution A and B				

Examp. No.	Formulation			Micromole	R
136	Solution A				
	Ciprofloxacin		100 mg	302	1.00
	Lactic acid 10% (w/w)		372 mg	413	1.37
	Hydrochloric acid		5.2 mg	142	0.47
	Water	ad	10.0 ml		
	Solution B				
	Sodium chloride		0.45 g		
	Water	ad	50.0 ml		
	Prepare the solution ready for use by mixing solution A and B				

Examp. No.	Formulation	Micromole R
37	<u>Solution A</u> Solution A from Example 65 <u>Solution B</u> Fructose 5.0 g Water ad 100.0 ml Prepare the solution ready for use by mixing solution A and B	
38	<u>Solution A</u> Solution A from Example 65 <u>Solution B</u> Ringer lactate solution: 250 ml (for example Ringer lactate DAB 7 manufactured by Braun Melsungen Rote Liste 1985 No. 51013) Prepare the solution ready for use by mixing solution A and B	
39	<u>Solution A</u> Solution A from Example 65 <u>Solution B</u> Mannitol 25.0 g Water ad 500.0 ml Prepare the solution ready for use by mixing solution A and B	

Examp. No.	Formulation			Micromole R	
40	<u>Solution A</u>				
	Ciprofloxacin		250mg	754	1.00
	Lactic acid 20% (w/w)		465 mg	1032	1.37
	0.1 M hydrochloric acid solution		1.63 ml	163	0.22
	Sodium chloride		173 mg		
	Water	ad	25 ml		
	<u>Solution B</u>				
	Glucose		5.0 g		
	Water	ad	100.0 ml		
	Prepare the solution ready for use by mixing solution A and B				

Examp. No.	Formulation			Micromole R	
41	**Solution A**				
	Solution A from Example 72				
	Solution B				
	Sodium chloride		2.25 g		
	Water	ad	250 ml		
	Prepare the solution ready for use by mixing solution A and B				
42	**Solution A**				
	Ciprofloxacin lactate. 2 H_2O		276 mg	604	1.00 (containing an equimolar amount of lactic acid)
	Lactic acid 10% (w/w)		20 mg	22	0.037
	0.1 M hydrochloric acid solution		2.00 ml	200	0.33
	Water	ad	4.0 ml		
	Solution B				
	Mannitol		5.0 g		
	Water	ad	100.0 ml		
	Prepare the solution ready for use by mixing solution A and B				

Examp. No.	Formulation			Micromole R	
43	**Solution A**				
	Solution A from Example 74				
	Solution B				
	Glucose		25.0 g		
	Water	ad	250.0 ml		
	Prepare the solution ready for use by mixing solution A and B				
44	**Solution A**				
	Solution A from Example 74				
	Solution B				
	Sodium chloride		4.5 g		
	Water	ad	500.0 ml		
	Prepare the solution ready for use by mixing solution A and B				
45	**Solution A**				
	Ciprofloxacin		100 mg	302	1.00
	Lactic acid 20% (w/w)		168 mg	373	1.24
	Water	ad	1.00 ml		
	Solution B				
	Sodium chloride		0.45 g		
	Water	ad	50.0 ml		
	Prepare the solution ready for use by mixing solution A and B				

Examp. No.	Formulation			Micromole R	
46	**Solution A**				
	Solution A from Example 77				
	Solution B				
	Ringer lactate solution:		100 ml (for example Ringer lactate DAB 7 supplied by Braun Melsungen Rote Liste 1985 No. 51013)		
	Prepare the solution ready for use by mixing solution A and B				
47	**Solution A**				
	Ciprofloxacin		200 mg	604	1.00
	Lactic acid 25% (w/w)		257 mg	715	1.18
	Water	ad	1.00 ml		
	Solution B				
	Sodium chloride		0.9 g		
	Water	ad	100.0 ml		
	Prepare the solution ready for use by mixing solution A and B				

Examp. No.	Formulation			Micromole	R
48	**Solution A**				
	Ciprofloxacin		175 mg	528	1.00
	Lactic acid 20% (w/w)		300 mg	667	1.26
	Water	ad	0.5 ml		
	Solution B				
	Glucose		2.5 g		
	Water	ad	50.0 ml		
	Prepare this solution ready for use by mixing solution A and B				
49	**Solution A**				
	Ciprofloxacin		200 mg	604	1.00
	Lactic acid 20% (w/w)		322 mg	715	1.18
	Hydrochloric acid		3.3 mg	90	0.15
	Sodium chloride		0.9 g		
	Water	ad	100.0 ml		
	Solution B				
	Solution for supplying amino acids: 500 ml (for example Aminoplasmal LS-5 electrolyte-free, supplied by Braun Melsungen, Rote Liste 1985 No. 51238)				
	Prepare the solution ready for use by mixing solution A and B				

Examp. No.	Formulation			Micromole	R
50	<u>Solution A</u>				
	Ciprofloxacin		100 mg	302	1.00
	Lactic acid 2% (w/w)		1481 mg	329	1.09
	Phosphoric acid		16 mg	165	0.50
	Water	ad	10.0 ml		
		pH:	3.8		
	<u>Solution B</u>				
	Sodium chloride		3.6 g		
	Water	ad	400 ml		
	Prepare the solution ready for use by mixing Solution A and B				

Examp. No.	Formulation			Micromole	R
51	<u>Lyophilizate</u>				
	Ciprofloxacin		100 mg	302	1.00
	<u>Solution</u>				
	Lactic acid 10% (w/w)		322 mg	358	1.18
	Hydrochloric acid		1.6 mg	45	0.15
	Sodium chloride		900 mg		
	Water	ad	100.0 ml		
	Prepare solution ready for use by dissolving the lyophilizate in the solution				
52	<u>Lyophilizate</u>				
	Ciprofloxacin lactate		63.6 mg	151	1.00 (containing an equimolar amount of lactic acid)
	<u>Solution</u>				
	Lactic acid 0.005% (w/w)		10.87 g	6	1.04
	Sodium chloride		225 mg		
	Water	ad	25 ml		
	Prepare solution ready for use by dissolving the lyophilizate in the solution				

Examp. No.	Formulation		Micromole	R
53	**Lyophilizate**			
	Ciprofloxacin lactate	127 mg	302	1.00 (containing an equimolar amount of lactic acid)
	Lactic acid	1,1 mg	12	0.04
	Mannitol	5,0 g		
	Solution			
	Water ad	100,0 ml		
	Prepare solution ready for use by dissolving the lyophilizate in the solution			
54	**Lyophilizate**			
	Ciprofloxacin	100 mg	302	1.00
	Solution			
	Lactic acid 20% (w/w)	186 mg	413	1.37
	0.1 M hydrochloric acid solution	0,42 ml	142	0.47
	Glucose	25,0 g		
	Water ad	500,0 ml		
	Prepare solution ready for useby dissolving the lyophilizate in the solution			

Examp. No.	Formulation		Micromole	R
55	<u>Lyophilizate</u>			
	Ciprofloxacin lactate	222 mg	604	1.00 (containing an equimolar amount of lactic acid)
	Glucose	12,5 g		
	<u>Solution</u>			
	Lactic acid 20% (w/w)	100 mg	222	0.37
	Hydrochloric acid	10,4 mg	284	0.47
	Water	ad 250 ml		
	Prepare solution ready for use by dissolving the lyophilizate in the solution			

Examp. No.	Formulation		Micromole R	
56	<u>Lyophilizate</u>			
	Ciprofloxacin lactate	222 mg	604	1.00 (containing an equimolar amount of lactic acid)
	Lactic acid	10 mg	111	0.18
	Mannitol	5,0 g		
	<u>Solution</u>			
	Water	100.0 ml		
	Prepare solution ready for use by dissolving the lyophilizate in the solution			
57	<u>Lyophilizate</u>			
	Lyophilizate from Example 92			
	<u>Solution</u>			
	Water	200,0 ml		
	Prepare solution ready for use by dissolving the lyophilizate in the solution			

Patent Claims

1. Infusion solutions of 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-quinoline-3-carboxylic acid (= ciprofloxacin) containing 0.015 to 0.5 g of the active compound per 100 ml of aqueous solution and, depending on the active compound concentration, 1.04 to 2.20 mol, relative to 1 mol of active compound, of one or more physiologically tolerated acids, and where when several acids are present their total content does not exceed the amount of 2.20 mol, relative to 1 mol of active compound.

2. Infusion solutions according to Claim 1, containing 0.015 to 0.5 g of the active compound per 100 ml of aqueous solution and an amount, which suffices to dissolve the active compound and to stabilize the solution, of one or more acid(s) from the group comprising hydrochloric acid, methanesulphonic acid, propionic acid, succinic acid, glutaric acid, citric acid, fumaric acid, maleic acid, tartaric acid, glutamic acid, gluconic acid, glucuronic acid, galacturonic acid, ascorbic acid, phosphoric acid, nitric acid, acetic acid, malic acid, L-aspartic acid and lactic acid, preference being given to lactic acid and hydrochloric acid or mixtures of lactic acid and hydrochloric acid.

3. Infusion solution according to Claim 2, containing 0.015 to 0.5 g of the active compound and 1.04 to 1.40 mol, relative to 1 mol of active compound, of lactic acid.

4. Infusion solutions according to Claim 2, containing 0.015 to 0.5 g of the active compound per 100 ml of aqueous solution and 1.12 to 1.24 mol, relative to 1 mol of active compound, of lactic acid.

5. Infusion solutions according to Claim 2, containing 0.015 to 0.5 g of the active compound per 100 ml of aqueous solution and up to 5 mol, relative to 1 mol of active compound, of lactic acid and another physiologically tolerated acid, with the proviso that the total amount of acid is, depending on the active compound concentration, more than 1.04 mol but does not exceed

2.20 mol, relative to 1 mol of active compound.

6. Infusion solutions according to Claims 1 to 5, characterized in that they contain thickeners, resorbents, light protection agents, absorption inhibitors, crystallization accelerators, absorption accelerators, crystallization retardants, complexing agents, antioxidants, isotonicizing agents and/or euhydrogenation agents as formulating auxiliaries.

7. Infusion solutions according to Claims 1 to 6 having an osmolality of 0.20 to 0.70 Osm/kg, preferably 0.26 to 0.39 Osm/kg, containing isotonicizing agents such as NaCl, sorbitol, mannitol, glucose, sucrose, xylitol, fructose and glycerol or mixtures of such substances and/or, where appropriate, substances which are contained as constituents in conventional infusion vehicle solutions.

8. Infusion solutions according to Claims 1 to 7, whose pH is 3.0 to 5.2.

9. Infusion solutions according to Claims 1 to 7 whose pH is 3.6 to 4.7, in particular 3.9 to 4.5.

10. Infusion solutions according to Claims 1 to 7, whose pH is 4.1 to 4.3.

11. Infusion solutions according to Claim 2, characterized in that, in addition to water, active compound and other formulating auxiliaries, they contain an amount of sodium chloride, or other auxiliaries customary for isotonicizing, such that the solution is in a form which is isotonic, or slightly hypo- or hypertonic, with the tissue fluid in the human or animal body.

12. Infusion solutions according to Claim 1, characterized in that, in addition to active compound, water and other formulating auxiliaries, they contain 1.04 to 1.40 mol of lactic acid and 0.0 to 0.80 mol of hydrochloric acid (in each case relative to 1 mol of active compound), and, relative to 100 ml of solution, 0.6 to 2.2 g of NaCl, preferably 0.75 to 1.20 g, in particular 0.85 to 0.95 g of NaCl.

13. Infusion solutions according to Claims 1 to 12 in dosage units which are suitable for infusion and which

can be prepared both from glass or from plastics suitable for this purpose, having removable contents of 40 to 600 ml, preferably from 50 to 120 ml.

14. Lyophilizates obtained by a freeze-drying process, and concentrates or other presentations which, before administration, can be converted into infusion solutions according to Claims 1 to 16.

15. Process for the preparation of infusion solutions, containing 0.015 to 0.5 % by weight of 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-quinoline-3-carboxylic acid (= ciprofloxacin), characterized in that a suitable amount of the active compound, where appropriate in the form of a salt, such as an alkali metal or alkaline earth metal salt or addition salt, of a hydrate or of a hydrate of the salt, or in the form of mixtures of these salts or hydrates, is mixed with the amount of a physiologically tolerated acid or of a mixture of several physiologically tolerated acids which, in relation to the amount which just suffices to dissolve the active compound or its salts or hydrates, represents an excess preventing separation out of the active compound, formulating auxiliaries are added where appropriate, and the mixture is made up with water or a customary infusion vehicle solution in such a manner that the concentration of the active compound is adjusted to the range from 0.015 to 0.5 g, and when an alkali metal or alkaline earth metal salt of the active compound is used the amounts of acid necessary for the dissolution additionally contain the amounts which are needed to neutralize the active compound anion, and when addition salts are used a part of the amounts of acid which are necessary is already contained in the active compound salt to be used.

16. Process according to Claim 15, characterized in that, in the case where the active compound is used in salt form, use is made of an acid whose anion corresponds to the anion of the active compound salt or salt hydrate.

17. Process according to Claim 15, characterized in that the active compound is, where appropriate, suspended

in water, and up to 5 mol, relative to 1 mol of active compound, of lactic acid are added, and then, where appropriate, another physiologically tolerated acid or a mixture of such acids, in particular hydrochloric acid, is added, with the proviso that the total amount of acid does not exceed 2.20 mol, relative to 1 mol of active compound, but does exceed 1.04 mol, relative to 1 mol of active compound, and then, where appropriate, further formulating auxiliaries are added, in particular NaCl, which is also, where appropriate, produced by a neutralization reaction in the formulation mixture, and the desired active compound concentration is adjusted by making up with water.

18. Process according to Claims 15 to 17, characterized in that the pH of the infusion solutions is adjusted to 3.0 to 5.2, in particular 3.6 to 4.7, with (physiologically) tolerated buffer systems.

19. Process according to Claims 15 to 18, characterized in that the infusion solutions are prepared by heating.

20. Use of infusion solutions and/or other presentations which, before administration, are converted into the infusion solutions according to Claims 1 to 14 for the preparation of dosage units which are suitable for infusion and have removable contents of 40 to 600 ml.