(19) INTELLECTUAL PROPERTY OFFICE

(11) Publication number: **NZ 237904 A**

(41) Publication date: **25.06.1993**

(51) Int. Cl: **A61K31/085; A61K9/22; A61K9/52;**

(12) Patent Application

(21) Application number: **NZ19910237904**

(22) Date of filing: **22.04.1991**

(30) Priority: **19900010039 GB 03.05.1990**

(71) Applicant(s): **RECKITT & COLMANN PROD LTD**

(72) Inventor(s): **DETTMAR PETER WILLIAM**
LLOYD-JONES JOHN GARETH

(54) **Title:**
GASTRIC SUSTAINED RELEASE COMPOSITIONS COMPRISING TRICLOSAN

These gastric sustained release compositions of triclosan for the treatment of gastrointestinal disorders associated with Helicobacter pylori infections comprise (1) a solid dosage form containing: 200 to 600 mg of alginic acid and/or a sodium, potassium, or magnesium salt thereof; 50 to 250 mg of a sodium or potassium carbonate or bicarbonate salt; 1 to 100 mg triclosan; and optionally up to 100 mg calcium carbonate; (2) an aqueous form containing 0.1 to 2% w/v triclosan; 1 to 8% w/v sodium or potassium alginate; 1.3 to 6.5% w/v of a sodium of potassium carbonate or bicarbonate salt; 0.5 to 4% w/v calcium carbonate; and optionally 0.3 to 1.7% w/v carbomer; or (3) a granular or spheroidal form containing triclosan and optionally a pharmaceutically acceptable carrier, coated with a mucoadherent polymer. Triclosan is of the formula:

New Zealand Patent Specification for Patent Number 237904

237904

Priority Date(s): 3.5.90
Complete Specification Filed: 22.4.91
Class: A61K31/1085; A61K9/22,52
Publication Date: 25 JUN 1993
P.O. Journal, No: 1369

NO DRAWINGS

NEW ZEALAND

PATENTS ACT, 1953

No.:

Date:

COMPLETE SPECIFICATION

GASTRIC SUSTAINED RELEASE COMPOSITIONS

I / We, **RECKITT & COLMAN PRODUCTS LIMITED**, a British company of One Burlington Lane, London, United Kingdom, W4 2RW

hereby declare the invention for which I / we pray that a patent may be granted to me/us, and the method by which it is to be performed, to be particularly described in and by the following statement:-

(followed by page 1a)

PREPARATION OF A MEDICAMENT

This invention relates to the preparation of a medicament for the treatment of gastrointestinal disorders associated with Helicobacter pylori infections.

The relationship between peptic ulcer disease and gastritis has been recognised for several decades. The relationship between gastritis and infection with Helicobacter pylori (formerly Campylobacter pylori), first demonstrated by Warren and Marshal in 1983, is now equally well established, see Vaira et al (Current Opinion in Gastroenterology 1989, 5: 817-823). Given this connection it is now being recognised that treatments of gastritis and peptic ulcer must be capable of removing the associated Helicobacter pylori infections.

A number of different treatment regimens have been proposed to treat Helicobacter pylori infections. European Patent applications No 206626 and 206627 (Marshall) describe the use of bismuth salts whilst EP 206625 (Marshall) and WO 86/05981 (Borody) describe the use of a combination of bismuth with a single antibiotic for the treatment of Helicobacter pylori. However, bismuth alone achieves low (30 to 70%) initial clearance rates for Helicobacter pylori and recurrence of the infection approaches 100% by twelve months post therapy. Bismuth together with a single antibiotic, namely amoxicillin, appears to be relatively effective as a short term means of reducing the symptoms but it is now clear that the use of bismuth together with a single antibiotic frequently fails to eradicate the

infection and has a high rate of reinfection (Rauws, Erik A.J. et al, Gastroenterology, 1988, 94: 33-40). WO 89/03219 (Borody) describes the use of a combination of bismuth, a first antimicrobial agent and a second antimicrobial agent. This treatment regimen is not only complicated and expensive but still has unacceptably high relapse rates.

A second approach to combination therapy uses histamine-H_2 receptor blocking anti-secretory agents. European Patent applications 282132 and 282131 (Proctor and Gamble) describe the use of H_2 antagonists in combination with bismuth or Campylobacter inhibiting antimicrobial agents. This approach has still led to high relapse rates and may lead to many of the undesirable side effects of the individual treatment components.

European Patent application No 219912 (Norwich Eaton) describes the use of nitrofurantoin as a monotherapy for the treatment or prophylaxis of infectious gastrointestinal disorders caused or mediated by Campylobacter-like organisms. This approach has been replaced in common practice by more complex duo or triple therapy.

There is still a requirement for an effective monotherapy of gastrointestinal disorders associated with Helicobacter pylori.

We have now investigated the in vitro activity of various non-antibiotic antimicrobial agents versus Helicobacter pylori.

Triclosan (2-hydroxy-4,2',4'-trichloro-diphenyl ether)

is described and claimed, along with various formulations, in GB Patents 1022744, 1024022 and 1038185, published in 1966. Whilst GB 1022744 claims that triclosan may be used for "oral administration to disinfect the intestinal and urinary tracts" very few details are given, and no specific infections or conditions are mentioned. Since these patents were published Applicant is not aware of any publications suggesting the use of triclosan in the treatment of any gastrointestinal diseases, nor have there been any suggestions that triclosan may have activity against gastrointestinal infections with Helicobacter pylori or any of the associated disease conditions.

According to the present invention there is provided the use of triclosan for the preparation of a medicament for the treatment of gastrointestinal disorders associated with Helicobacter pylori infections.

The effective oral dose of triclosan will depend upon the severity of the condition to be treated. Generally the dosage employed will fall within the range of 1 to 200mg and for most patients will fall within the range 10 to 100mg, for example 25mg. The frequency of dosing will again be dependent upon the severity of the condition to be treated and its sensitivity to the treatment, the dosing normally being up to three times a day.

The medicaments will be for oral administration and may be in the form of powders, granules, spheroids, tablets, capsules, solutions or suspensions.

For ease of administration and for accuracy in dosing,

the medicament may be prepared in unit dosage forms. Thus in the case of powders, granules or spheroids they may be conveniently packed into sachets, each unit containing, from 1 to 100mg (preferably 10 to 60mg) triclosan. In the case of tablets or capsules each unit will contain from 1 to 100mg (preferably 10 to 60mg) triclosan.

The medicament in the form of granules may be prepared by standard methods such as wet or dry granulation (slugging). They may be effervescent or non-effervescent to be mixed with a suitable quantity of water for administration as a drink. They may also be chewable granules.

The medicaments in the form of spheroids may be prepared by the following method. The triclosan and a carrier (for example microcrystaline cellulose) plus any other excipients are mixed with a sufficient quantity of water to form a 'plastic' wet mass. The mass is extruded into cylinders of uniform diameter and equal length. The extrudates are rolled into spheres using a spheroniser and then dried, preferably in a fluid bed dryer.

The medicaments in the form of powders may be prepared by blending the triclosan and one or more pharmaceutically acceptable excipients such as bulking agents/diluents.

The medicaments in the form of tablets may be prepared by standard methods such as granulation or direct compression. They may be buffered and effervescent or non-effervescent.

The medicaments in the form of capsules may be prepared

by standard methods such as filling powders, granules or spheroids into hard gelatine capsules or adding triclosan to melted pharmaceutically acceptable excipients before filling into capsules.

The medicaments in the form of solutions or suspensions may be prepared by mixing the components with a liquid such as water. Conveniently the liquid formulations will contain 1 to 100mg of triclosan in 5 to 20ml. They may include pharmaceutically acceptable conventional excipients such as suspending agents, buffer systems etc. In order to protect the medicaments against microbial deterioration it is preferable to include a preservative. A suitable system is a combination of methyl- and propyl- para-hydroxybenzoate (methyl and propyl parabens).

The medicaments may also include one or more of a colourising, sweetening or flavouring agent.

In another aspect of the invention the medicaments may be formulated as gastric sustained release compositions, having prolonged residence time within the stomach and continuously releasing triclosan during that time. In this aspect the medicaments may be formulated so as to produce floating alginate rafts within the stomach, or as muco-adherant-coated granules or spheroids.

Medicaments formulated so as to produce floating alginate rafts within the stomach may be in solid single dosage form as tablets, or in liquid form.

In the form of tablets the alginate containing gastric sustained release compositions of triclosan will comprise

200 to 600mg of alginic acid and/or a salt thereof, preferably a sodium, potassium or magnesium salt; 50 to 250mg of a sodium or potassium carbonate or bicarbonate salt; 1 to 100mg, preferably 10 to 60mg, triclosan; and optionally up to 100mg calcium carbonate. The compositions may also contain standard tableting excipients known in the art, such as soluble fillers, binders, lubricants and flavours. The tablets may be produced by standard procedures such as direct compression or by wet or dry granulation followed by tablet compression.

In the form of liquids the alginate containing gastric sustained release compositions of triclosan will comprise an aqueous medium containing 0.1 to 2% w/v triclosan; 1 to 8% w/v sodium or potassium alginate; 1.3 to 6.5% w/v sodium or potassium carbonate or bicarbonate salt; 0.5 to 4% calcium carbonate and optionally 0.3 to 1.7% w/v of a suspending agent, preferably carbomer. These liquid compositions may also contain standard excipients known in the art such as preservatives, flavouring and colouring agents. The alginate containing liquids may be produced by dispersing all of the ingredients except carbomer in water. If carbomer is used it will be added to the dispersion as a neutralised suspension in water.

When the alginate compositions described above come into contact with the, normally, acid conditions of the stomach the carbonate or bicarbonate salts produce effervescence, which aerates the raft structure formed by the alginates, causing it to float. It has, however, been

noted that in some patients suffering from Helibacter pylori infections the pH of the stomach contents may be elevated (possibly to as high as pH6) reducing effervescence and, consequently, reducing the ability of the rafts to float. Floating rafts may still be formed in such patients however either by, in the case of tablet compositions, further including a pharmaceutically acceptable, solid carboxylic acid, or an acid salt thereof in a sufficient amount to neutralise between one quarter and all of the carbonate and/or bicarbonate of the composition; or, in the case of tablet or liquid compositions, co-administering such an acid or acid salt. A suitable acid is citric acid.

Mucoadherent-coated granules or spheroids may be produced by forming triclosan containing granules or spheroids as described above, and coating them with one or more known mucoadherent polymers such as carboxymethyl-celllulose or sodium carboxymethylcellulose, carbomer (especially carbomer 934P), tragacanth, sodium alginate, methylcellulose, hydroxyethylcellulose, poly (ethylene oxide) or hydroxypropylmethylcellulose. The coating may be carried out by any conventional technique, for example spray coating. Once coated and dried the granules or spheroids may be filled into sachets or gelatine capsules or, if sufficiently robust microadherent coatings have been used, compressed to form tablets.

The invention is illustrated by the following examples.

EXAMPLE 1

Tablet

A preparation in the form of tablets was prepared according to the following formula

Triclosan	200g
Microcrystalline cellulose	1000g
Magnesium stearate	6g

The materials were blended together and compressed into tablets using 8mm diameter concave punches. Individual tablets had a weight of 301.5mg and contained 50mg triclosan.

EXAMPLE 2

Suspension

A preparation in the form of a suspension was prepared according to the following formula

Triclosan	1.0% w/v
Sodium carboxymethylcellulose	3.0% w/v
Propyl parabens	0.06% w/v
Methyl parabens	0.14% w/v
Peppermint flavour	0.1% w/v
Sodium saccharin	0.05% w/v
Water to	100%

The triclosan, parabens, flavouring and saccharin were dispersed in the bulk of the water. The sodium carboxymethylcellulose was added and stirred vigorously until dissolved. Water was added to bring the suspension to final volume and the suspension was mixed until it was homogenous.

EXAMPLE 3

Buffered tablets

A preparation in the form of buffered tablets was prepared according to the following formula

Triclosan	50g
Sodium carbonate	300g
Microcrystalline cellulose	600g
Modified cellulose gum	30g
Magnesium stearate	5g

The ingredients were blended together and then compressed using 13mm diameter normal concave punches to a weight of 985mg. Each tablet contained 50mg of triclosan.

EXAMPLE 4

Capsules

A preparation in the form of capsules was prepared according to the following formula

Triclosan	150g
Polyethyl glycol 6000	to 1050g

The polyethylene glycol was melted and the triclosan was added and stirred until dissolved. The melt was dosed into appropriately sized hard gelatine capsules such that each capsule contained 10, 50 or 100mg triclosan.

EXAMPLE 5

Solution

A preparation in the form of a solution was prepared according to the following formula

Triclosan	1%	w/v
Propylene glycol	20%	w/v
Polyethylene glycol 300	3%	w/v
Propyl paraben	0.0375%	w/v

Example 5 (contd)

Methyl paraben	0.03%	w/v
Flavour	qs	
Glycerol	to 100%	

The propylene glycol and polyethylene glycol were mixed and the triclosan was added and stirred until dissolved. The remaining ingredients were added and stirred until dissolved.

EXAMPLE 6

Effervescent tablets

A preparation in the form of effervescent tablets was prepared according to the following formula

Triclosan	50g
Sodium carbonate	100g
Citric acid	250g
Sodium bicarbonate	400g
Sorbitol direct compression grade	1000g
Maltodextrin	200g
Peppermint flavour	50g
Sodium saccharin	25g
Magnesium stearate	10g

The citric acid, sodium bicarbonate and 200g of the sorbitol were mixed in a planetary mixer and granulated with a small amount of water. The granules were dried in a fluid bed dryer and then passed through a 780µm mesh sieve. The remaining ingredients were added and blended together by tumble mixing. The mixture was compressed using 18mm

punches to a final tablet weight of 2085mg. Each tablet contained 50mg triclosan.

EXAMPLE 7

Sachets

A preparation in the form of sachets was prepared according to the following formula

Triclosan	100g
Citric acid	200g
Sodium bicarbonate	800g
Sodium carbonate	200g
Sorbitol	7000g
Sodium saccharin	100g
Peppermint flavour	200g

The ingredients were blended together and filled into sachets such that each sachet contained 50mg triclosan.

EXAMPLE 8

Capsules

A preparation in the form of capsules was prepared according to the following formula

Triclosan	5g
Microcrystalline cellulose	44g
Talc (sterilised)	1g

The powders were blended together and filled into appropriatly sized hard gelatin capsules such that each capsule contained 10, 25 or 50mg triclosan.

EXAMPLE 9

Alginate containing tablets

A gastric sustained release preparation in the form of

alginate containing tablets was prepared according to the following formula

	per batch	per tablet
	g	mg
Triclosan	200	50
Alginic acid FD (Protan)	2000	500
Sodium bicarbonate	680	170
Calcium carbonate	320	80
Mannitol	6092	1523
Magnesium stearate	100	25
Polyvinyl pyrrolidone (PVPk30)	400	100
Flavour peppermint Ferm 57.279	200	50
Sodium saccharin	8	2

All the ingredients other than the triclosan, magnesium stearate and the polyvinyl pyrrolidone were sieved and mixed in a planetary mixer. The polyvinyl pyrrolidone was dissolved in 2.7 litres of isopropyl alcohol and used to granulate the mixed powders. The granules were dried in a fluid bed dryer at 70°C for 30 minutes then sieved. The triclosan and magnesium stearate were blended into the granules and the mixture was compressed using 25mm punches to a final tablet weight of 2.5g. Each tablet contained 50mg triclosan.

EXAMPLE 10

Alginate containing tablets

A gastric sustained release preparation in the form of alginate containing tablets was prepared according to the following formula

	per batch	per tablet
	g	mg
Triclosan	20.45	50
Alginic acid LF-60 (Protan)	204.70	500
Sodium bicarbonate	69.60	170
Calcium carbonate	32.75	80
Citric acid	69.60	170
Mannitol	623.50	1523
Magnesium stearate	10.25	25
Flavour peppermint Ferm 57.279	20.45	50
Sodium saccharin	0.80	2

All the ingredients with the exception of the citric acid and magnesium stearate were sieved and mixed in a planetary mixer at a low speed setting. 250ml of deionised water were then introduced and the mixing speed increased, mixing continued for 3 minutes. The resultant granules were dried in an oven at 100°C for 40 minutes and then sieved. The citric acid and magnesium stearate were blended into the granules and the resultant mixture was compressed using 25mm punches to give 2.57g tablets each containing 50mg triclosan.

EXAMPLE 11

Alginate containing suspension

A gastric sustained release preparation in the form of an alginate containing suspension was prepared according to the following formula

	per batch	% w/v

	g	
Triclosan	250	0.5
Carbomer 934P	325	0.65
Sodium alginate SF120 (Protan)	750	1.5
Sodium bicarbonate	1335	2.67
Calcium carbonate	800	1.6
Methyl paraben	200	0.4
Propyl paraben	30	0.06
20% Sodium hydroxide(w/v) approx	650	1.3
Deionised water	to 50 L	to 100%

The carbomer was fully dispersed in approximately 20 litres of the deionised water. 20% w/v sodium hydroxide was added to bring the pH to between 7.0 and 7.2. The sodium alginate was dispersed in a separate 20 litres of deionised water and the sodium bicarbonate, parabens and calcium carbonate were added and stirred until homogenous. The gelled, neutralised carbomer was added to the alginate dispersion and mixed until homogenous. The triclosan was added and mixed and the batch was adjusted to final volume with deionised water.

EXAMPLE 12

Carbomer coated spheroids

A gastric sustained release preparation in the form of capsules containing carbomer-coated spheroids was prepared according to the following formula procedure.

Spheroids were prepared according to the following formula

per batch

Microcrystalline cellulose	2500g
Triclosan	500g

The powders were blended for 15 minutes, following which a total of 950ml of deionised water was added in aliquots whilst stirring continued at a slow speed. When the water had been incorporated the speed was increased for 2 minutes. The wet mass was extruded through a perforated screen of 1mm diameter holes using a Nica extruder (Nica Systems, Sweden). The wet extrudates were spheronised using a Nica spheroniser at 650rpm for 5 minutes. The spheroids were dried at 50°C for 1 hour.

A coating suspension was produced according to the following formula

Carbomer 934P	60.0g
Polyethylene glycol 6000	60.0g
Citric acid	56.25g
Deionised water	3000.00ml

The citric acid and polyethylene glycol were dispersed in 2250ml of the deionised water. The carbomer was added and dispersed by stirring at 2000rpm. The solution was made to volume by the addition of the rest of the water.

The dried triclosan spheroids were coated with the coating suspension using an Aeromatic Strea 1 fluid bed system and a spray nozzle diameter of 1.1mm. All of the suspension was used to coat the 3Kg of cores.

The coated spheroids were dried and filled into hard gelatine capsules such that each capsule contained 25mg of triclosan.

EXAMPLE 13

Sodium carboxymethylcellulose-coated spheroids

A gastric sustained release preparation in the form of capsules containing sodium carboxymethylcellulose-coated spheroids was produced according to the following procedure.

Triclosan containing spheroids were produced as described in Example 12.

A coating suspension was produced according to the following formula

Sodium carboxymethylcellulose (low viscosity grade)	60g
Polyethylene glycol 6000	60g
Deionised water	3000ml

The sodium carboxymethylcellulose and polyethylene glycol were sequentially dispersed in 2400ml of the deionised water by stirring at 2000rpm. The solution was made up to volume by the addition of the rest of the water.

The triclosan cores were coated with the above suspension using the method of Example 12, all 3 litres of suspension were used for the 3Kg of cores.

The coated spheroids were dried and filled into hard gelatine capsules such that each capsule contained 25mg of triclosan.

The *in vitro* activities of a range of antimicrobial compounds versus *Helicobacter pylori* were determined by methods based on those of McNulty et al (Antimicrobial Agents and Chemotherapy, 28, 837-838, 1985). The Minimum Inhibitory concentrations for 50% and 90% of the strains

used (MIC50 and MIC90), versus each antimicrobial were determined using an agar dilution technique.

The MIC of an antimicrobial agent was defined as that concentration (in mg per litre of agar) at which less than 1 in 10^5 organisms produced visible colonies.

Helicobacter pylori strains were isolated from gastric antrum biopsy specimens taken at routine endoscopy during investigation of upper gastrointestinal symptoms. They were identified as Helicobacter pylori by their colonial morphology, gram stain appearance and positive rapid urease test. The organisms were stored in liquid nitrogen before use and subcultured for testing by 48 hour incubation, at 37°C under 10% carbon dioxide in Tryptone Soya Broth (TSB, OXOID, UK) plus 5% horse serum (Tissue Culture Services, UK).

The first test procedure determined the effectiveness of a range of antimicrobial substances versus 16 to 18 strains of Helicobacter pylori at neutral pH. Freshly prepared Isosensitest Agar of pH 7.2 (Oxoid, UK) supplemented with 10% saponinlysed horse blood was used to prepare a dilution series of each antimicrobial from which agar plates were produced. A multipoint inoculator (Denley-Tech, UK) was used to deliver 1µl of undiluted test culture to the surface of each plate in the dilution series to give approximately 10^6 cfu/spot. The plates were incubated for three days at 37°C in a microaerobic atmosphere of 6% oxygen and 10% carbon dioxide.

Table 1 presents test data for the twelve selected

antimicrobial agents tested against Helicobacter pylori at neutral pH.

TABLE 1 - presents MIC50 and MIC90 values of twelve antimicrobial agents against eighteen isolates of Helicobacter pylori

	MIC (mg/l)		
Antimicrobial Agent	MIC50	MIC90	Range
Triclosan	1	8	0.25-16
Tinidazole	0.5	16	0.25-16
Cetalkonium Cl	2	4	2-4
Cetyl pyridinium Cl	8	8	8
Clioquinol	16	16	8-16
Hexetidine	16	16	8-16
Dichlorphen	16	16	8-16
Halquinol	16	16	16
4-Hexylresorcinol	32	32	16-32
Hibitane	32	32	16-32
PCMX	32	64	8-64
Guaiacol	64	64	32-128

From Table 1 it can be seen that triclosan with an MIC50 of 1mg/l and an MIC90 of 8mg/l, and tinidazole with an MIC50 of 0.5mg/l and an MIC90 of 16mg/l, demonstrated the greatest activity of the twelve antimicrobial agents tested. A reported MIC90 for bismuth subcitrate at neutral pH is 16mg/l.

Three of the antimicrobial agents were selected for further evaluation over the pH range of 5 to 8, a range at which Helicobacter pylori survives. The three selected

agents were triclosan, clioquinol (5-chloro-7-iodo-8-hydroxy-quinolone) and cetalkonium chloride. Tinidazole was rejected at this stage due to an observed bimodal distribution of MICs. Fifteen of eighteen isolates were sensitive with an MIC of less than 2mg/l, the other three strains demonstrating evidence of resistance with an MIC of 16mg/l. This bimodal distribution has previously been reported with metronidazole, another imidazole. In the clinical situation, acquired resistance to the nitro-imidazoles can occur in many strains of Helicobacter pylori after only three weeks treatment, therefore, this agent would not be recommended for the treatment of Helicobacter pylori associated gastrointestinal disorders.

The MIC90s of the three selected antimicrobial agents were determined for sixteen to eighteen clinical isolates of Helicobacter pylori over the pH range 5 to 8. In the test procedure, Sorensens phosphate buffer (0.1M) was used to prepare the range of pH values 5, 5.5, 6, 6.5, 7, 7.5 and 8. Oxoid Columbia Agar Base (CM331) was added and the media autoclaved. After cooling to 50°C, 7% Lysed Horse Blood (Tissue Culture Services, UK) was added and media at each pH was used to prepare a range of concentrations of the three selected test antimicrobial agents. To ensure pH stability, a surface pH electrode was used to monitor control plates before, during and at the end of the three day microaerobic incubation.

The MIC90 was determined for each at each pH as described in the previous test procedure.

Tables 2-4 present the test data using the above test procedure.

TABLE 2 - presents the effect of pH on the activity (MIC90 mg/l) of triclosan against sixteen isolates of Helicobacter pylori

pH Value	MIC90 (mg/l)	Range (mg/l)
5.0	0.25	0.06-0.25
5.5	1	0.06-1
6.0	1	0.12-2
6.5	2	0.12-4
7.0	2	0.06-4
7.5	2	0.06-4
8.0	2	0.06-2

From Table 2 it can be seen that the MIC90 for triclosan was low at pH 5.0 and unaffected in the range pH 5.5 to 8.0.

TABLE 3 - presents the effect of pH on the activity (MIC90 mg/l) of clioquinol against sixteen isolates of Helicobacter pylori

pH Value	MIC90 (mg/l)	Range (mg/l)
5.0	2	0.5-4
5.5	8	2-8
6.0	8	2-8
6.5	8	0.5-16
7.0	2	0.5-4
7.5	2	0.5-4
8.0	1	0.5-2

From Table 3 it can be seen that the activity of

clioquinol was only slightly affected by pH. The difference would not be clinically important.

TABLE 4 - presents the effect of pH on the activity (MIC90 mg/l) of cetalkonium chloride against eighteen isolates of Helicobacter pylori

pH Value	MIC90 (mg/l)	Range (mg/l)
5.0	1	0.5-2
5.5	2	0.5-2
6.0	2	1-4
6.5	4	2-4
7.0	4	2-4
7.5	4	1-4
8.0	2	1-8

Cetalkonium chloride was largely unaffected by pH over the range 5 to 8.

Of the antimicrobial agents evaluated over a range of pH from 5 to 8, triclosan demonstrated the greatest activity with an MIC90 of 0.25mg/l (range 0.06-0.25) at pH 5. The activity of the other two agents, clioquinol and cetalkonium chloride, demonstrated similar MIC90 activity profiles across the pH range.

What we claim is:-

1. A gastric sustained release composition of triclosan for the treatment of gastrointestinal disorders associated with *Helicobacter pylori* infections in a solid unit dosage form comprising 200 to 600mg of alginic acid and/or a sodium, potassium or magnesium salt thereof; 50 to 250mg of a sodium or potassium carbonate or bicarbonate salt; 1 to 100mg triclosan; and optionally up to 100mg calcium carbonate.

2. A composition as claimed in Claim 1 wherein each unit contains 10 to 60mg triclosan.

3. A composition as claimed in Claim 1 or Claim 2 further including a pharmaceutically acceptable solid carboxylic acid or an acid salt thereof; in a sufficient amount to neutralise between one quarter and all of the carbonate and/or bicarbonate of the composition.

4. A composition as claimed in Claim 3 wherein the acid is citric acid.

5. An aqueous gastric sustained release composition of triclosan for the treatment of gastrointestinal disorders associated with *Helicobacter pylori* infections comprising 0.1 to 2% w/v triclosan; 1 to 8% w/v sodium or potassium alginate; 1.3 to 6.5% w/v of a sodium or potassium carbonate or bicarbonate salt; 0.5 to 4% w/v calcium carbonate; and optionally 0.3 to 1.7% w/v carbomer.

6. A gastric sustained release composition of triclosan for the treatment of gastrointestinal disorders associated with *Helicobacter pylori* infections in the form of granules or spheroids comprising triclosan, and optionally a pharmaceutically acceptable carrier, coated with a mucoadherent polymer.

7. A gastric sustained release composition as claimed in Claim 6 wherein said mucoadherant polymer is selected from the group consisting of carboxymethylcellulose, sodium carboxymethylcellulose, carbomer, tragacanth, sodium alginate, methylcellulose,

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hydroxyethylcellulose, poly (ethylene oxide) ~~or~~ and hydroxypropylmethyl-cellulose.

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8. A gastric sustained release composition of triclosan substantially as described in any one of Examples 9 to 13.

9. An aqueous gastric sustained release composition as defined in claim 5 substantially as herein described with reference to any examples thereof.

Reckitt & Colman Products Limited
By His/~~Her~~/Their Authorised Agents,
A. J. PARK & SON
Per .....

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