

Señor Jefe

DIVISION DE NUEVAS CREACIONES

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

Santa Fe de Bogotá, D.C.

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Re.: 02-01-09
Expediente No. 00 - 30.256

Solicitud de Patente

SMITHKLINE BEECHAM CORPORATION

Debidamente traducida adjunto acompaño la copia oficial de la solicitud de patente básica Estadounidense No. UK 09/301.838 la cual le solicito agregar a este expediente para los efectos legales respectivos.

De Usted atentamente,

GERMAN CASTILLO GRAU

T.P.#2.978 del C.S.J.

ESTADOS UNIDOS DE AMÉRICA

A TODOS A QUIENES LLEGUE EL PRESENTE:

DEPARTAMENTO DE COMERCIO DE LOS ESTADOS UNIDOS

Oficina de Marcas y Patentes

14 de febrero de 2000.

LA PRESENTE CERTIFICA QUE LA ADJUNTA ES UNA COPIA TOMADA DE LOS REGISTROS DE LA OFICINA DE MARCAS Y PATENTES DE LOS ESTADOS UNIDOS, DE LOS DOCUMENTOS DE LA SOLICITUD DE PATENTE ABAJO IDENTIFICADA Y LA CUAL CUMPLE CON LOS REQUISITOS PARA QUE LE SEA CONFERIDA UNA FECHA DE RADICACIÓN SEGÚN 35 USC 111.

NÚMERO DE SOLICITUD 09/301,838

FECHA DE RADICACIÓN: 29 de abril de 1999

Por Autoridad del

COMISIONADO DE MARCAS Y PATENTES

(FIRMA) P. SWAIN

Oficial de Certificaciones

(SELLO DORADO DE OBLEA)

FORMULACIONES FARMACÉUTICAS

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REIVINDICACIONES:

1. Una tableta masticable que comprende trihidrato de amoxicilina en el cual la base masticable consiste esencialmente de manitol presente en al menos 25% por peso de la tableta.
2. Una tableta según la reivindicación 1 adaptada para ser administrada a un paciente pediátrico.
3. Una tableta según la reivindicación 1, en la cual la tableta se provee en una forma de dosis aja que comprende aproximadamente entre 150 y 250 mg de amoxicilina y una forma de dosis alta que comprende aproximadamente entre 350 y 450 mg de amoxicilina.
4. Una tableta según la reivindicación 1, en la cual amoxicilina está presente entre 45 y 60% por peso de la tableta.
5. Una tableta según la reivindicación 1, en la cual manitol está presente entre 30 y 50% por peso de la tableta.
6. Una tableta según la reivindicación 1, que además comprende excipientes, por ejemplo, desintegrantes, lubricantes, agentes endulcorantes, agentes colorantes y saboreantes.
7. Una tableta según la reivindicación 1, en la cual un desintegrante puede estar presente entre 1 y 4% por peso de la tableta.

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8. Una tableta según la reivindicación 1, en la cual el desintegrante es crospovidona.
9. Una tableta según la reivindicación 1, en la cual un lubricante puede estar presente entre 0,25 y 2,0% por peso de la tableta.
10. Una tableta según la reivindicación 9, en la cual el lubricante es estearato de magnesio.
11. Una tableta según la reivindicación 1 en la cual el agente endulcorante es un agente endulcorante artificial.
12. Una tableta según la reivindicación 11, en la cual el agente endulcorante artificiales aspartame.
13. Una tableta según la reivindicación 3 en la cual la tableta de dosis baja tiene un peso total entre aproximadamente 400 y 500 mg y la tableta de dosis alta tiene un peso total entre aproximadamente 850 y 950 mg.
14. Una tableta masticable que comprende entre aproximadamente 50 y 55% de trihidrato de amoxicilina; entre 40 y 45% de manitol; entre 1 y 2% de desintegrante; entre 0,5 y 1,2% de lubricante; entre 0,5 y 1,5% de agente endulcorante artificial; y agentes saboreantes y colorantes.
15. Un método para el tratamiento de infección bacteriana en un paciente pediátrico que consiste en administrar a dicho paciente una cantidad efectiva de una tableta según la reivindicación 1.
16. Un método según la reivindicación 14, en el cual la dosis es administrada cada 12 horas.

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17. Un gránulo farmacéutico que comprende trihidrato de amoxicilina presente entre 45 y 60% por peso del gránulo y manitol presente en 25% por peso del gránulo.
18. Un gránulo según la reivindicación 18, que además comprende un desintegrante presente entre 1 y 4% por peso del gránulo.
19. Un gránulo según la reivindicación 18, que además comprende un lubricante presente entre 0,125 y 1,0% por peso del gránulo.
20. Un gránulo según la reivindicación 18, que comprende trihidrato de amoxicilina presente entre 50 y 55%, manitol presente entre 40 y 45%, crospovidona presente entre 1 y 2% y estearato de magnesio entre 0,25 y 0,6% todo en % por peso del gránulo. }
21. Una tableta masticable que comprende gránulos compuestos por trihidrato de amoxicilina presente entre 45 y 60% por peso del gránulo y manitol presente entre 25% por peso del gránulo.
22. Una tableta masticable según la reivindicación 20 que además comprende un lubricante extragranular, presente en aproximadamente 50% de la cantidad total del lubricante en la tableta.

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THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

February 14, 2000

**THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM
THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK
OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT
APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A
FILING DATE UNDER 35 USC 111.**

APPLICATION NUMBER: 09/301,838

FILING DATE: April 29, 1999



**By Authority of the
COMMISSIONER OF PATENTS AND TRADEMARKS**

**P. SWAIN
Certifying Officer**

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UTILITY PATENT APPLICATION
TRANSMITTAL

Attorney Docket No. P32295
First Named Inventor or Application Identifier
Davidson et al.

(For new nonprovisional applications under 37 CFR 1.53(b))

"EXPRESS MAIL CERTIFICATE"

"EXPRESS MAIL" MAILING LABEL NUMBER EL175487801US DATE OF DEPOSIT: APRIL 29, 1999

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.53(b) on the date indicated above and is addressed to The Assistant Commissioner for Patents, Box Patent Application, Washington, D.C. 20231.

NAME OF PERSON MAILING PAPER OR FEE

BY OR PRINT LYNN S. MORRISON

SIGNATURE

[Signature]

04/29/99
09/30/98
04/29/99

APPLICATION ELEMENTS

1. ☒ MPEP chapter 600 concerning utility patent application contents.

The Commissioner is hereby authorized to charge indicated fees and credit any overpayments to Deposit Account No. 19-2570

☒ General Authorization to charge any and all fees under 37 CFR 1.16 or 1.17, including petitions for extensions of time, relating to this application. (37 CFR 1.136(a)(3))
(Submit an original, and a duplicate for fee processing)

2. ☒ The total fee is calculated as shown below:

Basic Filing fee \$760.00
Total Claims 22 - 20 = 2 x \$18 \$ 36.00
Independent Claims 4 - 3 = 1 x \$78 \$ 78.00
☐ Multiple Dependent Claims present. \$260
TOTAL FILING FEE \$874.00

☐ Cancel in this application original claims to of the prior application before calculating the filing fee.

☒ Charge \$874.00 to the above indicated Deposit Account.

3. ☒ Specification excluding Drawings [Total Pages] 11

4. ☐ Drawing(s) (35 USC 113) [Total Sheets] 0

5. ☒ Declaration and Power of Attorney [Total Pages] 2

a. ☐ Newly executed (original or copy)
b. ☐ Copy from a prior application (37 CFR 1.63(d))
(for continuation/divisional with Box 17a completed)
c. ☒ Unsigned Declaration

(Note Box 6 below)

i. ☐ DELETION OF INVENTOR(S)

Signed statement attached deleting inventor(s) named in the prior application, see 37 CFR 1.63(d)(2) and 1.33(b).

6. ☐ Incorporation By Reference (useable if Box 5b is checked)

The entire disclosure of the prior application, from which a copy of the oath or declaration is supplied under Box 5b, is considered as being part of the disclosure of the accompanying application and is hereby incorporated by reference therein.

7. ☒ The Title of the Invention:

PHARMACEUTICAL FORMULATIONS

8. ☐ Nucleotide and/or Amino Acid Sequence Submission

a. ☐ Computer Readable Copy
b. ☐ Paper Copy (identical to computer copy)
c. ☐ Statement verifying identity of above copies
d. ☐ Use the identical computer-readable form filed in Application No. _____, filed _____ as the computer-readable form for the instant application. (37 CFR 1.821(e))

9. ACCOMPANYING APPLICATION PARTS

a. ☐ Information Disclosure Statement (IDS)
b. ☐ PTO-1449
c. ☐ Copies of all IDS Citations

10. ☐ Assignment Papers (cover sheet & document(s))

11. ☐ Prior Application is Assigned to:

(for continuation/divisional with Box 17a completed)

12. ☐ Preliminary Amendment [Total Pages]

13. ☒ Return Receipt Postcard (MPEP 503)
(Should be specifically itemized)

14. ☐ Certified Copy of Priority Document(s)
(If foreign priority is claimed)

15. ☐ Transfer all references cited by Applicants or by the Examiner from the parent Application Serial No. _____ filed _____ A
PTO-1449 listing the references is enclosed.

16. ☐ Other: _____

17. ☐ Priority Information, check appropriate box and supply the requisite information

a. The accompanying application is a ☐ Continuation ☐ Divisional ☐ Continuation-in-part (CIP)
of prior application No: 0 filed 0.

b. ☐ Benefit is claimed under Title 35, United States Code, Section 119(e) of the following Provisional Applications:
Application No. _____ filed _____

c. ☐ Please amend the specification by inserting before the first line the sentence: (37 CFR 1.78)

This is a continuation/divisional of application Serial No. _____ filed _____

18. CORRESPONDENCE ADDRESS

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19. RESPECTFULLY SUBMITTED,

Signature
Name

[Signature]
Dara L. Dinner

Registration No. 33,680

Attorney Docket No.: P32295

Pharmaceutical Formulations

5 Field of The Invention

The present invention relates to novel pharmaceutical formulations comprising amoxycillin.

Background of The Invention

- 10 Amoxycillin is an anti-bacterial agent extensively used for the treatment of a wide range of bacterial infections. It is currently available in a number of different formulations, for instance, as capsules, chewable tablets, oral suspensions and paediatric drops. Different formulations and different amounts of amoxycillin are provided for adult and paediatric patients. Thus, for example, SmithKline Beecham
- 15 market, under the trade mark "Amoxil", *inter alia* chewable tablets comprising either 125mg or 250mg amoxycillin, for adult patients, and, for paediatric patients, an oral suspension comprising either 125mg or 250mg/5 ml of suspension. Existing formulations are approved for dosing at least three times a day (tid). These chewable tablets contain a substantial amount of sugar (about 21% by weight) which makes the
- 20 tablet base less suited for adaption to a paediatric tablet. In addition, SmithKline Beecham also market, under the trade mark "Augmentin", *inter alia* chewable tablets comprising 125mg amoxycillin and 31.25mg potassium clavulanate or 250mg amoxycillin and 62.5mg potassium clavulanate, for administration to adult patients.
- 25 EP 0 396 335-A1 (Beecham Group plc) describes chewable effervescent tablets, for instance a "fizzy chewable" tablet comprising amoxycillin (250mg) in which the chewable base comprises a mixture of sorbitol and mannitol, present in about 15% and 31% by weight of the tablet, respectively. The effervescent couple helps mask the unpleasant bitter taste of amoxycillin. A disintegrant such as a cellulose product
- 30 may also be present, in an amount from 5 to 30%, to give the patient the option of dispersing the tablet in a small amount of water prior to administration.
- WO 92/19227 (Laboratorios Beecham SA) describes swallow tablets comprising amoxycillin which are prepared from granules formed by roller compaction of
- 35 amoxycillin with a disintegrant.

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There still remains a need to provide further formulations comprising amoxycillin, which provide an alternative to existing formulations and which may also provide for a more convenient dosage regimen, especially for children.

5 Summary of the Invention

The present invention provides for a chewable tablet comprising amoxycillin trihydrate in which the chewable base comprises essentially mannitol which is present in at least 25% by weight of the tablet.

10 Detailed Description of the Invention

The present invention provides for a chewable tablet preferably adapted for administration to a paediatric patient.

15 The tablet is also preferably provided for in both a low amount dosage form and a high amount dosage form. Conventionally, the amount of amoxycillin trihydrate present in a dosage form is expressed as the weight of the corresponding free acid amoxycillin. Preferably, the low dosage form comprises from about 150 to 250 mg, more preferably 175 to 225mg, typically about 200mg amoxycillin. Preferably, the high dosage form comprises about 350 to 450, more preferably 375 to 425mg, typically about 400mg amoxycillin.

20 Preferably, the amoxycillin trihydrate is present in either dosage form from about 45 to about 60%, more preferably from about 50 to about 55% by weight of the tablet.

25 Preferably, mannitol is present from about 30 to about 50%, more preferably from about 35 to about 45%, yet more preferably from about 40 to about 45%, by weight of the tablet. Preferably, a granular grade of mannitol is used.

30 For manufacturing convenience, it is preferred to maintain a constant tablet weight. Preferably, the amount of mannitol is adjusted to compensate for any variation in the amount of amoxycillin trihydrate, on account of the purity thereof. Preferably, amoxycillin trihydrate and mannitol together comprise from about 90 to about 97%, more preferably about 92 to about 96%, yet more preferably about 93 to about 96% by weight of the tablet.

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5 In addition to an excipient to provide a chewable base, a tablet according to the present invention may also comprise further excipients, for instance, disintegrants, lubricants, sweetening agents, colouring and flavouring agents. Such further excipients together will preferably comprise from 3 to 10%, more preferably 4 to 8%, yet more preferably 4 to 7% by weight of the tablet.

10 Disintegrants may be present in from 1 to 4%, preferably from 1 to 3%, more preferably from 1 to 2% by weight of the tablet. Representative disintegrants include crospovidone, sodium starch glycolate, starches such as maize starch and rice starch, croscarmellose sodium and cellulose products such as microcrystalline cellulose, microfine cellulose, low substituted hydroxy propyl cellulose, either used singly or in admixture. Preferably, the disintegrant is crospovidone. The presence of a disintegrant such as crospovidone in the tablet is found to produce a dramatically faster dissolution rate.

15 Lubricants may be present in from 0.25 to 2.0%, preferably from 0.5 to 1.2% by weight of the tablet. Preferred lubricants include magnesium stearate.

20 Preferably, the sweetening agent is an artificial sweetening agent such as sodium saccharin or aspartame, preferably aspartame, which may be present in from 0.5 to 1.5% by weight of the tablet. Preferably, a tablet of the present invention is substantially free of sugar (sucrose).

25 Preferred flavouring agents include fruit flavours which may be natural or synthetic, for instance peppermint, cherry and banana, or a mixture thereof. Preferably, a tablet of the present invention is substantially free of a flavour enhancer such as glycine.

30 Preferably, the low dosage tablet has a total weight in the range 400 to 500mg, more preferably 425 to 475mg, typically about 450mg. Preferably, the high dosage tablet has a total weight in the range 850 to 950mg, more preferably 875 to 925mg, typically about 900mg.

35 In a preferred embodiment, a tablet of the present invention comprises from 50 to 55% amoxycillin trihydrate; from 40 to 45% mannitol; from 1 to 2% disintegrant, preferably, crospovidone; from 0.5 to 1.2% lubricant, preferably magnesium stearate;

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from 0.5 to 1.5% artificial sweetening agent, preferably aspartame; and flavouring and colouring agents, the % being expressed as % of the weight of the tablet.

5 Preferably, the chewable tablets of the present invention are used for treating a wide range of bacterial infections in paediatric patients, such as infections of the ear, nose and throat, infections of the genitourinary tract, infections of the lower respiratory tract and skin and soft tissue infections. Preferably, the unit dosage is taken every 12h (bid, q12h). This provides a more convenient dosage regimen for a paediatric patient, as there is no need to dose the child during the middle of the day, when the
10 child may be at school.

15 Tablets of the present invention may be prepared by blending together the various excipients together with amoxycillin by conventional techniques, for example by direct compression. Alternatively, some of the ingredients may be first slugged or subjected to roller compaction and resultant slugs or flakes then milled to form granules. These granules are then blended with the remaining ingredients and finally compressed into tablets. The preparation of granules comprising amoxycillin trihydrate has previously been described in WO 92/19227 (Laboratorios Beecham SA) and in WO 98/35672 (SmithKline Beecham Laboratoires Pharmaceutiques). In
20 a preferred process, granules are prepared by roller compaction and then milling from a primary blend comprising amoxycillin trihydrate, mannitol, the disintegrant and about 50% of the lubricant. The granules are then blended with the remaining lubricant and any remaining other excipients to form a secondary blend which is then and compressed into tablets. Preferably, the sweetening and colouring agents are
25 incorporated into the primary blend while the flavouring agents are incorporated into the secondary blend.

Granules formed with mannitol are novel. Accordingly, in another aspect the present invention provides for granules comprising amoxycillin trihydrate present in from
30 about 45 to about 60%, more preferably 50 to 55% by weight of the granule and mannitol present in from about 25%, preferably 30 to 50%, more preferably 35 to 45%, yet more preferably 40 to 45%, by weight of the granule.

Preferably, the granules further comprise a disintegrant as hereinbefore described,
35 present in from 1 to 4%, preferably from 1 to 3%, more preferably from 1 to 2% by weight of the granule.

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Preferably, the granules further comprise a lubricant as hereinbefore described, present in 0.125 to 1.0%, preferably from 0.25 to 0.6% by weight of the granule.

5 Preferred granules comprise amoxycillin trihydrate present in from 50 to 55%, mannitol present in from 40 to 45%, crospovidone present in from 1 to 2%, and magnesium stearate present in from 0.25 to 0.6%; all percents (%) being by weight of the granule.

10 In a further aspect, the present invention provides for a chewable tablet comprising granules as hereinbefore described. Preferably, the tablets comprise an extra-granular lubricant, present in about 50% of the total amount of lubricant.

15 The chewable tablets are preferably packaged in sealed protective containers, such as screw cap bottles, plastic or metal tubes, aluminium foil sachets, aluminium blister packs, etc..

The invention is illustrated by the following Examples:

20 Example 1 - "200mg" tablet

	Amoxycillin trihydrate*	232.56mg	51.68%
	(equivalent to amoxycillin free acid	200)	
	Mannitol (granular)	190.93	42.43
25	Crospovidone	7.02	1.56
	Aspartame	3.24	0.72
	Magnesium stearate	4.50	1.00
	Colouring agent	0.27	0.06
	Flavouring agents	11.48	2.55
30	Total tablet weight	450	

*based on 86% potency (the "potency" being an adjustment to take account of for the purity and the trihydrate content). The quantity of mannitol is adjusted according to the potency of the amoxycillin trihydrate, in order to maintain a constant tablet
35 weight.

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Example 2 – "400mg" tablet

	Amoxycillin trihydrate*	465.12mg	51.68%
	(equivalent to amoxycillin free acid	400)	
5	Mannitol (granular)	381.87	42.43
	Crospovidone	14.04	1.56
	Aspartame	6.48	0.72
	Magnesium stearate	9.00	1.00
	Colouring agent	0.54	0.06
10	Flavouring agents	22.95	2.55
	Total tablet weight	900	

15 *based on 86% potency (the "potency" figure being an adjustment to take account of both the purity and the trihydrate content). The quantity of mannitol is adjusted according to the potency of the amoxycillin trihydrate, in order to maintain a constant tablet weight.

20 The tablets were prepared by initially blending together amoxycillin trihydrate, crospovidone, colouring agent, aspartame, mannitol and magnesium stearate (1/2 quantity). The blend was then processed by roller compaction and milled to form granules. These granules were blended with the flavouring agents and the remaining magnesium stearate and the overall blend compressed to form tablets.

25 Reference Example 1 – existing 250mg chewable tablet (Amoxil)*

Amoxycillin 250mg (as amox trihydrate)

30 Inactive ingredients: citric acid, cornstarch**, FD&C Red No. 40, flavorings, glycine, mannitol, magnesium stearate, saccharin sodium, silica gel and sucrose.

* Physicians Desk Reference, 49 edn, Medical Economics Data Production Co, Montvale NJ 07645-1742, 2351, 1995

** a constituent of the product comprising the flavourings

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~~44~~**Dissolution Assay**

The method used was that described in the The United States Pharmacopeia (USP 23, 1995) at page 104, for Amoxicillin and Clavulanate Potassium Tablets, adapted as follows:

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Apparatus: 2 (paddles)
RPM: 75
Media: 900 ml of 37° C water

10 For 200 and 400mg chewable tablets (Examples 1 and 2)

Time 30 min
Q 75%

For 125 and 250mg chewable tablets (Reference Example):

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Time 90 min
Q 80%

For Capsule formulation comprising amoxycillin:

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Apparatus: 1 (baskets)
RPM: 100
Media: 900 ml of 37° C water
Time: 90 minutes
Q = 80%

25 Thus, the presence in the chewable tablets of the present invention of a disintegrant, crospovidone, was found to dramatically increase the dissolution rate of the chewable tablet, compared with an existing chewable tablet (Reference Example 1) which does not have a disintegrant. There was 75% dissolution after 30 minutes, compared with 80% dissolution after 90 minutes. Furthermore, the chewable tablets of the invention

30 had an improved dissolution rate when compared to the existing Amoxil (Trade Mark) capsule formulation.

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Bioequivalence Study

In addition, in a bioequivalence study in human volunteers, the 400mg chewable tablet was demonstrated to be bioequivalent to a paediatric suspension of amoxycillin comprising a corresponding amount of amoxycillin per 5ml of suspension.

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All publications, including but not limited to patents and patent applications, cited in this specification are herein incorporated by reference as if each individual publication were specifically and individually indicated to be incorporated by reference herein as though fully set forth.

10

The above description fully discloses the invention including preferred embodiments thereof. Modifications and improvements of the embodiments specifically disclosed herein are within the scope of the following claims. Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. Therefore the Examples herein are to be construed as merely illustrative and not a limitation of the scope of the present invention in any way. The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows.

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What is Claimed Is:

1. A chewable tablet comprising amoxycillin trihydrate in which the chewable base comprises essentially mannitol which is present in at least 25% by weight of the tablet.
2. A tablet as claimed in claim 1 adapted for administration to a paediatric patient.
3. A tablet as claimed in claim 1 in which the tablet is provided in a low dosage form which comprises from about 150 to 250 mg amoxycillin and a high dosage form which comprises about 350 to 450mg amoxycillin.
4. A tablet as claimed in claim 1 in which amoxycillin is present in from 45 to 60% by weight of the tablet.
5. A tablet as claimed in claim 1 in which mannitol is present in from 30 to 50% by weight of the tablet.
6. A tablet as claimed in claim 1 which comprise further excipients, for instance, disintegrants, lubricants, sweetening agents, colouring and flavouring agents.
7. A tablet as claimed in claim 1 in which a disintegrant may be present in from 1 to 4% by weight of the tablet.
8. A tablet as claimed in claim 7 in which the disintegrant is crospovidone.
9. A tablet as claimed in claim 1 in which a lubricant may be present in from 0.25 to 2.0% by weight of the tablet
10. A tablet as claimed in claim 9 in which the lubricant is magnesium stearate.
11. A tablet as claimed in claim 1 in which the sweetening agent is an artificial sweetening agent.
12. A tablet as claimed in claim 11 in which the artificial sweetening agent is aspartame.

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13. A tablet as claimed in claim 3 in which the low dosage tablet has a total weight in the range 400 to 500mg and the high dosage tablet has a total weight in the range 850 to 950mg.

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14. A chewable tablet which comprises from 50 to 55% amoxycillin trihydrate; from 40 to 45% mannitol; from 1 to 2% disintegrant; from 0.5 to 1.2% lubricant; from 0.5 to 1.5% artificial sweetening agent; and flavouring and colouring agents.

10 15. A method of treating bacterial infection in a paediatric patient which comprises administering to said patient an effective amount of a tablet as claimed in claim 1.

16. A method as claimed in claim 14 in which the dosage is administered every 12h.

15 17. A pharmaceutical granule comprising amoxycillin trihydrate present in from 45 to 60% by weight of the granule and mannitol present in from 25% by weight of the granule.

20 18. A granule as claimed in claim 18 further comprises a disintegrant present in from 1 to 4% by weight of the granule.

19. A granule as claimed in claim 18 which further comprises a lubricant present in 0.125 to 1.0% by weight of the granule.

25 20. A granule as claimed in claim 18 which comprises amoxycillin trihydrate present in from 50 to 55%, mannitol present in from 40 to 45%, crospovidone present in from 1 to 2%, and magnesium stearate present in from 0.25 to 0.6%; all %s being by weight of the granule.

30 21. A chewable tablet comprising granules comprising amoxycillin trihydrate present in from 45 to 60% by weight of the granule and mannitol present in from 25% by weight of the granule.

35 22. A chewable tablet as claimed in claim 20 which further comprises and an extra-granular lubricant, present in about 50% of the total amount of lubricant in the tablet.

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Abstract

A chewable tablet comprising amoxycillin in which the chewable base comprises essentially mannitol which is present in at least 25% by weight of the tablet are useful
5 for treating a wide range of bacterial infections in children.

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DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

"Pharmaceutical Formulations"

the specification of which (check one)

☒ [X] is attached hereto.

☐ [] was filed on _____ as Serial No. _____

and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

☒ I acknowledge the duty to disclose information which is material to the patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

☒ I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) or Section 365(b) of any foreign application(s) for patent or inventor's certificate, or Section 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below any foreign application for patent or Inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed.

☒ Prior Foreign Application(s)

Number	Country	Filing Date	Priority Claimed

I hereby claim the benefit under Title 35, United States Code, Section 119(e) of any United States provisional application(s) listed below.

Application Number	Filing Date

I hereby claim the benefit under Title 35, United States Code, Section 120 of any United States application(s) or Section 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code, Section 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

Serial No.	Filing Date	Status

27 50


I hereby appoint the practitioners associated with the Customer Number provided below to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith, and direct that all correspondence be addressed to that Customer Number:

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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