

Identification of World Health Organisation ship's medicine chest contents by Anatomical Therapeutic Chemical (ATC) classification codes

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ABSTRACT

Background: Ships should carry mandatory given amounts of medicinal products and basic first aid items, collectively known as the ship's medicine chest. Type and quantities of these products/items are suggested by the World Health Organisation (WHO) and regulated by individual flag states. In countries that lack national legislation, it is assumed that ships should follow WHO indications. An objective difficulty mainly involving vessels of international long-haul routes could be to recognise medicinal compounds obtained in other countries for replacing products used or expired. Language barrier may complicate, if not make it impossible to interpret the name of the medicinal product and/or of the active principle as indicated in a box printed in a completely different language. Handling of the ship's pharmacy may be difficult in case of purchasing of drugs abroad due to language barriers. Medicinal products are identified by the international non-proprietary name of the active principle and/or by their chemical or invented (branded) names. This may make the identification of a medicinal product difficult, primarily if it is purchased abroad and the box and instructions are written in the language of the country where it is marketed. Therefore, there is a simpler classification system of the medicinal compounds the ATC (ATC: Anatomy, Therapeutic properties, Chemical, pharmacological properties). This paper has reviewed the list of medicinal products recommended by WHO and assigned to each one the ATC code as a solution to the problem of medicinal compounds organisation.

Materials and methods: Two researchers independently examined the list of medicinal compounds indicated in the third edition of the International Medical Guide for Ships and attributed to each compound the ATC code according to the 2013 Guidelines for ATC classification and Defined Daily Dose (DDD) assignment.

Results: The ATC code was attributed to the medicinal compounds indicated in the third edition of the International Medical Guide for Ships.

Conclusions: The availability of an objective system to identify medicinal products is required for ships, which will contribute in making the identification of items purchased simpler, making it easier to understand which drug seafarers need to be administer, and consequently reduce possible therapeutic mistakes.

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Key words: ATC code, medicine chest, ship's pharmacy, identification of medicinal compounds

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INTRODUCTION

The provision of good quality medical care for people on board seagoing vessels still represents a challenge for medicine as the majority of vessels do not have a doctor or adequately trained paramedic personnel on board. On the other hand, ships are at sea for days or weeks before they can reach a port. In this situation, the best possibility for treating diseases or injuries is to provide medical advices via telecommunication systems, to guarantee adequate training of personnel with the responsibility of health care on board and to have an adequate supply of medicinal products and medication items [1, 2]. Medicines and medical equipment available on board of a ship constitute the so-called “medicine chest”. Although, at present, in larger ships the medicine chest is no longer a chest, but rather a small pharmacy with a variety of medicinal products and medical devices, the name has remained in memory of the box containing some of the therapeutic aids of the past, that was kept on board, centuries ago by the captain, paramedics or physicians. The United States of America were probably the first country to mandate in 1790, that every American flag vessel over 150 tons with a crew of ten should to carry a medicine chest [3]. In the nineteenth century, probably in relation to the significant increase in maritime traffic, various states began to regulate the matter of hygiene on board ships. Some countries started to prescribe the presence of a medicine chest on ships. International regulations were introduced with the international health conference held in Paris at the end of 1851 [4]. This meeting lead to an agreement in force of which the contracting states undertook to check the hygienic condition of the vessels, the food ration, the health of the crew, and the presence of the “chest for medicinal products” with, attached, instructions for their use [4]. In a global world and taking into account that shipping is per se an international activity, the best solution is to approach the problem of the provision of the medical chest with a global view and commence efforts for the harmonisation of the contents of the ship pharmacy as much as possible. Ships should carry compulsorily given amounts of medicinal products and medication items. Type and quantities of these products/items are established by flag state regulations. The first attempt to address the problem of providing international ships with a minimum supply of medicinal products and medication items come from the World Health Organisation (WHO). In collaboration with the International Labour Office (ILO) WHO published in 1967, the first edition of the International Medical Guide for Ships with a final appendix in which the minimum provision of medicinal products required to be on board of all the world’s ships was indicated. This list was updated in 1988 with the second edition of the International Medical Guide for Ships [5] and in 2008, with the third and last edition

of the same book [6, 7]. Lacking national regulations, it is assumed that ships should follow WHO indications. Besides the discussion on the quality and quantity of medicines and medication items should be available on board ships [8], another practical problem especially for vessels involved in international long-haul routes could be to recognise medicinal products obtained in other countries for replacing products utilised or expired. Language barrier may complicate, if not make it impossible to interpret the name of the medicinal product and/or of the active principle as indicated in a box printed, in a completely different language. This is due to lack of a precise indication system to recognise the same pharmaceutical product in any part of the world. This is why the best solution of this problem could be the use, for the contents of ship medical chest, an accurate indication system such as the ATC code (The Anatomical Therapeutic Chemical Classification System) [9, 10]. The ATC is a classification system of drugs maintained by the Nordic Council on Medicine and WHO/WHO Collaborating Centre for Drug Statistics Methodology of Uppsala (Sweden) [9]. In the ATC system drugs are divided into several groups according to the target organ, the mechanism of action and chemical and therapeutic characteristics [11]. In this work we have attributed the ATC code to the medicinal products of the WHO list for making identification and storage of products irrespective of the country where they were obtained, simpler and efficient.

MATERIALS AND METHODS

The ATC classification system is based on the principle that each pharmaceutical product is associated with a single code. The drugs, therefore, must be classified according to their main therapeutic use. In the ATC system the drugs are divided into different groups according to the target organ, the mechanism of action and chemical and therapeutic characteristics [11]. Each main group is divided into five hierarchical levels as detailed in Table 1.

Based on the target organ of a therapeutic action, the ATC Anatomical Main Group is divided into 14 “Anatomical Main Groups” each indicated by a letter identifying the apparatus or system of organs on which the drug exerts its therapeutic action according to alphabetical order. The categories are listed in Table 2.

Two researchers independently (first analysis team) examined the list of medicinal compounds indicated in the third edition of the International Medical Guide for Ships [6] and attributed to each compound the ATC code according to the 2013 Guidelines for ATC classification and Defined Daily Dose (DDD) assignment [11] and the centralised human medicinal product by ATC code of the European Union [12]. A drug, however, can be used for two or more therapeutic indications of equal importance and this leads to different al-

Table 1. The five hierarchical levels of the ATC classification system

Level	Groups	Characteristic
I	The ANATOMIC GROUP	Characterised by a letter of the alphabet
II	GROUP THERAPY	Characterised by a 2-digit number
III	SUB THERAPEUTIC	Characterised by a letter of the alphabet
IV	SUB CHEMICAL/THERAPEUTIC	Characterised by a letter of the alphabet
V	SUB CHEMICAL	Characterised by a 2-digit number specific to each chemical

Table 2. Categories further dividing the ATC Anatomical Main Group based on the therapeutic action on the target organ

A	Alimentary tract and metabolism
B	Blood and blood-forming organs
C	Cardiovascular system
D	Dermatological
G	Genito-urinary system and sex hormones
H	Hormonal preparations, excluding sex hormones
J	Anti-infectives for systemic use
L	The antineoplastic and immunomodulating agents
M	Musculoskeletal system
N	Nervous system
P	Antiparasitic, insecticides and repellents
R	Respiratory system
S	Sensory organs
V	Various

ternatives for its classification. A drug may also be provided in two or more dosages or pharmaceutical forms for different therapeutic uses: the actual therapeutic use in such cases will determine the classification. Preparations that cannot be unequivocally classified in a particular group are coded to a level IV with the letter X. For the classification of such ambiguous cases, two researchers (second analysis team), were involved in the evaluation and allocation of ATC code and in consensus with the first two researchers, and based on the actual main therapeutic use, they were assigned a proper ATC code.

RESULTS

The ATC codes of medicines prescribed by WHO to be made available on board ships are shown divided for therapeutic classes. Table 3 summarises the ATC code for anti-inflammatory, anti-viral, anti-malarial drugs, antibiotic and anti-fungal agents. Table 4 indicates the ATC code for anti-allergic and anti-shock, cardiovascular and nervous system agents.

Table 5 lists the ATC codes for gastrointestinal, local anaesthetic, main analgesic, anti-haemorrhagic, anti-muscarinic, diuretic and hyperglycaemising agents recommended

by WHO to be carried on board ships. The ATC codes of other drugs are indicated in Table 6.

DISCUSSION

The problem of provisions of medicinal products on board ships is not simple due to the diversity of laws and regulations on the distribution and use of medicinal products for different countries. Several countries have updated in the last years the content of the ship's medicine chest for their own fleets [3, 13–16]. A comparative analysis of regulations and contents reveals significant non-homogeneity probably reflecting the different points of views in delivering assistance to patients. The international standard of the minimum provision of medicines that each ship must carry is reported as an appendix of the WHO International Medical Guide for Ships and the Medical First Aid Guide for use in Accidents Involving Dangerous Goods [6]. Ships usually undertake voyages, at times, far away from their own country for extended periods. Apart from the psychological problems that extended periods at sea, away from families can cause, the distance from the country of origin of the ship, which is common for vessels employed in international long-haul routes, can also cause problems in the supply of medicines for the ship's pharmacy. Regularly prescribed medicinal products cannot be mailed abroad and therefore the only possibility to obtain medical supplies is to purchase them in a port where the ship lands. This situation makes some practical problems for the handling agent to purchase medicines at a local pharmacy, to acquire same product required by the flag state of the ship or the difficulty, if not the impossibility for the seafarers to understand what medicinal compounds, are present inside the newly obtained medicines. For instance, medicinal products obtained in other countries with indications in foreign languages that the ship's officer may not be able to understand. As an example, extensively used, anti-hypertensive drug nifedipine in Chinese is '硝苯地平', in Greek is 'νιφεδιπίνη', in Russian is 'нифедипин', in Persian 'نیپیدیفن'. In this regard, if the supplier is not careful in providing indications in English or in the language of the ship's country, identification of a compound purchased abroad can be extremely difficult. Medicinal products are identified by the international

Table 3. ATC codes for anti-inflammatory, anti-viral, anti-malarial drugs, antibiotic and anti-fungal agents

Generic name	Therapeutic group	Possible trade names	Dosage form	ATC CODE V
Anti-inflammatory drugs				
Acetylsalicylic acid	Analgesic, anti-inflammatory	Aspirin, Aspro	Tablet 300 mg	N02BA01
Ibuprofen	Anti-inflammatory, antirheumatic non steroids	Advil, Actifen, Genpril, Haltran, Medipren, Brufen	Coated tablet 400 mg	M01AE01
Paracetamol Acetaminophen	Anti-fever and antalgic	Tylenol, Panadol	Tablet 500 mg	N02BE01
Hydrocortisone 1% cream	Anti-inflammatory and anti-allergic	NA	Cream	D07AA02
Prednisone	Corticosteroids for systemic use	Prednisolone	Tablet 25 mg	H02AB07
Anti-viral drugs				
Aciclovir	Antiviral	Zovirax, Acyclovir	Tablet 400 mg	J05AB01
Zidovudine plus Lamivudine	Antiviral (HIV)	Combivir	Tablet 300 mg + 150 mg	J05AR01
Anti-malarial drugs				
Artemether	Anti-malarial	Larither	Ampoule 1 mL = 80 mg	P01BE02
Artemether + Lumefantrine	Anti-malarial	Riamet	Tablets 2 mg + 120 mg	P01BF01
Antibiotic and anti-fungal agents				
Amoxicillin + clavulanate	Antibiotic	Augmentin, co-amoxyclav	Tablet 875 mg/125 mg	J01CR02
Azithromycin	Antibiotic	Zithromax	Tablet 500 mg	J01FA10
Ceftriaxone	Antibiotic	Rocephin	Ampoule 1 g powder for injection (dissolve in water for injection)	J01DD04
Ciprofloxacin	Antibiotic	Ciproxin, Cipro	Tablet 250 mg	J01MA02
Mebendazole	Anthelmintic, remedy for intestinal worms	Vermox	Tablet 100 mg	P02CA01
Metronidazole	Antiprotozoal	Flagyl	Tablet 500 mg	P01AB01
Miconazole 2% cream	Antifungal	Daktarin, Dermacure, Monistat	Cream	A01AB09
Tetracycline 1% ointment	Antibiotic	NA	Ointment	S01AA09
Doxycycline	Antibiotic with broad-spectrum antibacterial activity	Neo-Dagracycline, Unidox, Vibra-S, Vibramycine, Doryx	Tablet 100 mg	J01AA01

NA – not available

non-proprietary name of the active principle and/or by their chemical or invented (branded) names. The list of WHO [6] as well as the majority of flag states national lists [3, 13, 15–19] indicates medicinal products to be on board by the name of the active principle. Some explanations and brand names of the most common medicines are also elaborated [6, 17, 19]. Other lists such as the Norwegian, are more generic and indicate the categories of drugs required, without specific indication of names of medicinal compounds [14]. All these instructions are usually self-explanatory, but have the limitation in the correspondence, in case a medicine which has consumed or expired, and has to be replaced with another one obtained abroad. This apparently difficult situation can be easily solved, if that is the one next to the generic name of the active ingredient which is international, as used throughout the world, the addition of the ATC code

definitely increase security. In this way they will avoid many identification errors, often due also to lack of clarity in the international treaties which should serve as a reference. As a reference to this point “paracetamol” that in International Medical Guide for Ships third edition is also labelled as acetaminophen, on the contrary generic name of the drug known as paracetamol in Europe is referred to as acetaminophen in the United States and Canada. The ATC classification system is based on the principle that each pharmaceutical preparation is associated with a single code and drugs are classified according to their main therapeutic use. In case a drug can be used for two or more therapeutic indications of equal importance, this leads to different alternatives for its classification. A drug may also be provided in two or more dosages or pharmaceutical forms for different therapeutic uses: the actual therapeutic use in such cases will deter-

Table 4. ATC codes for anti-allergic and anti-shock, cardiovascular and nervous system agents

Generic name	Therapeutic group	Possible trade names	Dosage form	ATC CODE V
Anti-allergic and anti-shock agents				
Cetirizine	Anti-histaminic, anti-allergic	Zyrtec	Tablet 10 mg	R06AE07
Dexamethasone	Anti-allergic, anti-asthmatic, anti-anaphylactic shock	Decadron	Ampoule 4 mg/mL	H02AB02
Salbutamol	Anti-asthma, anti-chronic bronchitis, anti-emphysema	Albuterol, Ventolin, Proventil	Inhaler 0.1 mg/dose with volume spacer	R03AC02
Cardiovascular agents				
Adrenaline	Cardiac stimulants, anti-anaphylactic shock, anti-asthma	Epinephrine, Adrenaline 1:1000	Ampoule 1 mL = 1 mg	C01CA24
Isosorbide dinitrate	Anti-angina and anti-cardiac failure	Cedocard, Isordil	Tablet 5 mg	C01DA08
Metoprolol	Anti-hypertension; anti-atrial fibrillation	Selokeen, Lopresor, Toprol XL, Betaloc	Tablet 100 mg	C07AB02
Nervous system agents				
Diazepam	Anxiolytic	Valium	Tablet 5 mg	N05BA01
Midazolam	Anxiolytic	Hypnovel	Ampoule 1 mL = 5 mg	N05CD08
Haloperidol	Antipsychotic	Haldol	Ampoule 1 mL = 5 mg	N05AD01

mine the classification [11, 12]. The preparations which cannot be unequivocally classified in a given group are encoded to a level IV with the letter X. A medicinal product may be used for two or more equally important indications, and the main therapeutic use of a drug may differ from one country to another. This will often give several classification alternatives. Such drugs are usually only given one code, the main indication being decided on the basis of the available literature. For example, the preparations of nifedipine are classified with C08CA05 code, where: C indicates the cardiovascular system (level I), C08 – calcium (level II), C08C – selective calcium antagonists with predominant vascular effects (level III), C08CA – dihydropyridine derivatives (level IV) and C08CA05 – nifedipine (level V). Pharmaceuticals are classified on the basis of main therapeutic use, following the principle that all similar formulations, comparable to ingredients, unit dose and route of administration, may have only one ATC code. The indication of the ATC code in the list of medicinal compounds required to be on board ships will offer the advantage not only of an easy identification of the product irrespective of the place where it has been obtained. It will be also useful to place a proper order of a given medicinal compound when stocks have been sold or expired. Moreover, the identification through ATC system also facilitates the initiation of a review of the contents of the medicine chest given by the WHO in International Medical Guide for Ships third edition. ATC attribution queues could justify or contradict, the presence of some active principles using the system. For example misoprostol, as can be seen from the ATC code: A02BB01, A refers to the prostaglandin analogue, primarily used to prevent and

not treat gastric and duodenal ulcers and not simply as a prevention of postpartum haemorrhage, as indicated by International Medical Guide for Ships third edition. In addition to emergency physicians in the United States, the prevention and treatment of severe bleeding after childbirth is an off-label in the sea, child-birth is very rare on the sea and therefore the presence of this drug in this indication makes little relevance. Vitamin K is also another example of a drug included by International Medical Guide for Ships third edition for its use as a haemostatic in case of bleeding caused by the use of warfarin (anticoagulant), although warfarin is rarely used in the ships, which also makes the presence of vitamin K on board ships questionable. At the present the only flag state national list reporting besides to the classic list per therapeutic principle the ATC code is the Italian one [20]. This represents a real progress and a relevant effort for making handling of the ship's pharmacy easier and more effective.

An alternative strategy to ATC code, due to the difficulty for seafarers, who often lack proper technical prowess of ATC code interpretation, could be achieved by replacing in the computer each letter that makes up the specific ATC code (from A to Z) with a two-digit number based on its position in the alphabet: A = 01, B = 02, C = 03, D = 04V = 22, Z = 26, so that each ATC code becomes a numeric sequence of ten digits. In this way, for example, paracetamol, whose ATC code is N02BE01 would be assigned the new code 1402020501. This identification strategy can be used only within the same company, as pharmacists around the world will have no familiarity with the system. Such a system has been used successfully for years by

Table 5. ATC codes for gastrointestinal, local anaesthetic, main analgesic, anti-haemorrhagic, anti-muscarinic, diuretic and hyperglycaemising agents

Generic name	Therapeutic group	Possible trade names	Dosage form	ATC CODE V
Gastrointestinal agents				
Ondansetron	Anti-vomiting, anti-seasickness	Zofran	Tablet 4 mg	A04AA01
Sodium chloride 0.9% infusion	Liquid replacement	NaCl 0.9%, saline solution	Plastic bottle, 1 L	A12CA01
Loperamide	Antidiarrheal	Imodium, Diacure	Tablet 2 mg	A07DA03
Oral rehydration salt	Anti-dehydration in diarrhoea	Repolyte, Gastrolyte, Dioralyte	Sachets of powder for reconstitution	A07CA
Omeprazole	Anti-peptic ulcer, anti-gastro-oesophageal, reflux	Losec, Prilosec	Tablet 20 mg	A02BC01
Docusate with Senna (or equivalent)	Anti-constipation	Coloxyl	Tablet 50 mg + 8 mg	A06AG10
Local anaesthetic agents				
Amethocaine 0.5% eye drops	Local anaesthetic	Tetracaine	Single-use vial 1 mL	S01HA03
Lignocaine 1% (without adrenaline)	Local anaesthetic	Xylocaine, Lidocaine	Ampoule 5 mL	N01BB02
Main analgesic agents				
Morphine (injectable)	Opioid analgesic (treatment severe pain)	NA	Ampoule 1 mL = 10 mg	N02AA01
Morphine (oral)	Opioid Analgesic (treatment of moderate to severe pain)	NA	Liquid 1 mg/mL	N02AA01
Naloxone	Antidote for opiate	Narcan	Ampoule 1 mL = 0.4 mg	V03AB15
Anti-haemorrhagic agents				
Misoprostol	Prevent postpartum haemorrhage	Cytotec	Tablet 200 mg	A02BB01
Vitamin K	Anti-bleeding caused by the use of warfarin	Konaktion, Phytomenadione	Ampoule 1 mL = 10 mg	B02BA01
Anti-muscarinic agents				
Atropine	Ophthalmologicals, mydriatics and cycloplegics	NA	Ampoule 1.2 mg/mL	S01FA01
Diuretic agents				
Furosemide	Diuretic	Lasix, Furosemide	Ampoule 4 mL = 40 mg	C03CA01
Hyperglycaemising agents				
Glucagon, ready to use	Glycogenolytic (used in severe hypoglycaemic crisis)	Glucagen	Ampoule 1 mg	H04AA01

NA – not available

some cruise companies which lists of medication are far more extensive than the WHO list. In these cases, the drugs have been listed through their ATC codes to 10 digits, accordingly, ships of the same company have their medicines organised in a uniform manner. Of course, introduction of such a new identification system of medicinal compounds on ships would require agreements and issuing guidelines from authoritative sources.

CONCLUSIONS

In this paper we have added the international ATC code to the WHO list of medicinal products to be present on board

ships [6]. This alphanumeric code will allow the purchase and identification of a product in any country of the world without the need to know the brand name of the drug that may be different from country to country. The adoption of a classification system such as the ATC by all national flag states would allow seafarers on any ship finding, in whatever country they are, necessary medications. This will allow moving towards a more universal system of classification of medicinal compounds for the ship's medicine chest. Last but not least, the adoption of this international standard will allow efficient organisation of the contents of the ship's medical chest by competent authorities without the need

Table 6. ATC codes for other (minor) agents not listed in Tables 3–5

Generic name	Therapeutic group (E.U.)	Possible trade names	Dosage form	ATC CODE V
Ethanol 70%, hand cleanser gel	Disinfectant (alternative hand washing)	NA	Gel	D08AX08
Ethanol 70%, liquid	Disinfectant	NA	Liquid	D08AX08
Charcoal, activated	Ingested poisons absorbent	NA	50 g in 300 mL purified water	A07BA01
Permethrin 1% lotion	Ectoparasiticides, scabicides	Loxazol, Elimite, Nix	Lotion	P03AC04
Permethrin 5% lotion	Ectoparasiticides, scabicides	Lyclear	Lotion	P03AC04
Povidone iodine ointment 10% and solution 10%	Anti-infectives and antiseptics	Betadine, Povidine	Ointment, liquid	G01AX11
Oxymetazoline 0.5% (or equivalent)	Nasal decongestion	Drixine	Drops	R01AA05
Fluorescein 1%, strips	Cornea damage detector	NA	NA	S01JA01
Zinc oxide	Protective for irritated skin	NA	Paste or ointment, 20%	D02AB

NA – not available

of relatively high level pharmacological competence that could be not always available.

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