Recurring confusion between opium tincture and paregoric

ISMP urges pharmacies, ambulatory care centers, physician practices, and other locations to take action immediately to minimize the risk of fatal confusion between opium tincture and paregoric (camphorated tincture of opium). Paregoric has been used for many years to control diarrhea in children and adults. However, it often is dangerously referred to by its synonym, camphorated tincture of opium, which can be confused easily with opium tincture. **Paregoric has just 0.4 mg/mL of morphine while opium tincture contains 10 mg/mL — a 25-fold difference!** This is a potentially dangerous situation that invites serious medication errors.

Last month we received a report from a woman whose father died three days after an apparent mix-up of these two medications. She informed us that her 85-year-old father had been prescribed “camphorated opium tincture 5 mL PO BID to TID until diarrhea stops.” Early in the day, the pharmacy delivered the prescription to the foster care home where her father resided. That evening he was unresponsive with labored breathing. The daughter found out later that the pharmacy had returned the same day with a new bottle of medication labeled “opium tincture 0.6 mL BID to TID until diarrhea stops,” and had taken back the original bottle. We suspect that the pharmacy initially dispensed opium tincture instead of “camphorated opium tincture” (paregoric) and the patient received several 5 mL doses before the error was recognized.

In another report, a 51-year-old woman with chronic diarrhea died from morphine intoxication after receiving one teaspoonful of opium tincture (about 50 mg morphine), typically dosed by the number of drops, instead of paregoric, which is dosed by teaspoonful. After one dose of opium tincture, the patient became weak, tired, and achy. Her son checked on her periodically, but when he tried to wake her later that day, she did not respond. Paramedics were summoned, but they could not revive the woman. The patient’s physician had prescribed “camphorated tincture of opium.” A recent pharmacy graduate confused this with opium tincture.

Safety Briefs

- In our last issue, we reported on precautions that should be taken now that the “New & Improved” KAOPECTATE contains bismuth subsalicylate instead of attapulgite. Since then, a physician reader reminded us that bismuth subsalicylate also can lead to darkened or black-colored stool. A patient reporting this finding might be misdiagnosed with sustained gastrointestinal bleeding if the practitioner is unaware of the change in formulation. Bismuth also commonly causes the tongue to appear black. Avoid this product in children and teenagers who have or are recovering from chicken pox or the flu (due to risk of Reye’s syndrome). Also avoid using this in patients with salicylate allergies or those taking aspirin or salicylate-containing drugs. In addition, this product may interact with warfarin, methotrexate, and other drugs that commonly interact with aspirin.

- A community pharmacist reported that a prescription for “SEROPHENE (clomiphene citrate) 10 mg daily for two weeks before menstrual period” was left on a telephone answering device. The dose and instructions made no sense to the pharmacist because clomiphene is available in 50 mg tablets and given as a daily 50 to 100 mg dose for a total of five days during a month to stimulate ovulation. When the pharmacist called the prescriber for clarification, an office nurse told him that Serophene was intended. But the pharmacist persisted and asked her to check with the doctor. The prescription was actually for SARAFEM (fluoxetine), which is available in 10 mg and 20 mg capsules and used once a day for premenstrual dysphoric disorder. Keep in mind that sound-alike confusions can occur with communications related to both prescribing and dispensing. Educate all staff involved in these communications that errors can be minimized by practices such as repeating and spelling back drug names, matching the patient’s condition to the drug’s indication, as well as prescriber clarification when orders are questionable. In addition, when answering devices are used, be sure to include prompts that ask callers to spell out drug names and provide the indication for use.
Opium tincture (cont’d from previous page)

ISMP received another report where a prescription for “DTO 0.7 mL PO q4h” was received by a community pharmacy for a recently discharged 13-day-old infant with a diagnosis of opiate withdrawal. The pharmacist processing the order interpreted this as deodorized tincture of opium (official name is opium tincture, deodorized). He attempted to verify the dose using standard drug information sources, but found the dose to be excessive. He called the hospital pharmacy for verification and discovered that “DTO” was an abbreviation for “diluted tincture of opium,” a 25-fold dilution of deodorized tincture of opium. While the newborn had been prescribed a morphine dose totaling 1.68 mg per day, she may have received 42 mg daily if “deodorized tincture of opium” had been dispensed. Thus, a 25-fold overdose was averted, which undoubtedly saved the infant’s life. The hospital pharmacy was made aware of the confusion caused by the use of “DTO” as an abbreviation for the diluted solution.

To reduce the risk of similar errors, discuss the following issues with staff members who may prescribe, dispense, or administer these medications at your practice site:

- Determine if there is a need to even stock opium tincture. Check the last time this medication was dispensed and eliminate it from the inventory if possible.
- In the US, paregoric (the official name for camphorated tincture of opium) should be the designated nomenclature used for prescriptions and for listing in inventories, computer systems, on labels, etc. Tell clinicians that it is dangerous to refer to paregoric as “camphorated tincture of opium.” Likewise, “DTO” should never be used as an abbreviation for opium tincture (also known as deodorized tincture of opium) because a 1:25 dilution has also been referred to as DTO (diluted tincture of opium).
- Build alerts into computer systems to proactively advise staff to review the prescription and dosing information. The alert should include appropriate dose ranges by weight and volume. If possible, also include the maximum dose.
- Because all who have access to opium tincture may not be familiar with its dangerous properties, place poison labels on all containers as well as a label stating the strength of morphine per mL (10 mg/mL) and a statement, “WARNING! Do NOT confuse opium tincture with paregoric.”
- Place auxiliary labels in pharmacy storage locations as a constant reminder.
- Dispense opium tincture only in small dropper bottles or oral syringes.
- Recognize that measuring opium tincture doses accurately may prove challenging. Provide appropriate measuring devices to accurately measure the correct dose.
- In neonatal abstinence syndrome due to opiate withdrawal, some pediatricians recommend opium tincture in a 1:25 dilution. This is similar to the amount of morphine in paregoric. But paregoric contains 45% alcohol and other potentially harmful ingredients. To eliminate the need for opium tincture, pharmacies should prepare an aqueous oral solution of morphine from soluble oral tablets or injection.
- Educate pharmacy, medical, and nursing students/recent graduates about these medications and the potential for life-threatening errors if they are confused.

Safety Briefs (cont’d from previous page)

- What’s the chance of receiving an error-free prescription dispensed from your local community pharmacy? About 98.3%, according to a new study (Flynn EA, Barker KN, Carnahan BJ. National observational study of prescription dispensing accuracy and safety in 50 pharmacies. J Am Pharm Assoc 2003;43:191-200). Put another way, with about 3 billion prescriptions dispensed each year in the US, a 1.7% chance of an incorrectly dispensed medication equates to about 51.5 million errors each year! Overall, the authors found about 4 errors each day in pharmacies dispensing 250 prescriptions per day. To perform the study, the doctor’s original paper prescription or computer-generated label (for refills) was compared to the contents and label of completed prescriptions. Based on prescription volume, 52% of the study facilities were chain pharmacies, 31% were independent pharmacies, and 17% were hospital outpatient pharmacies, collectively representing six US metropolitan areas. No significant differences in dispensing accuracy were found among pharmacy type or geographic area. Accuracy ranged from 87% (n=1) to 100% (n=13). Of 4,481 prescriptions evaluated, 77 errors (0.1%) were judged to be clinically important. Wrong label information and instructions were the most common types of errors. Although less serious than wrong drug errors, the authors caution pharmacists not to ignore these more common types of errors. The authors also recorded and published observed error prevention techniques used by one or more of the study pharmacies.
- We were recently notified by a pharmacist of a near miss due to look-alike confusion between bottles of metronidazole (generic equivalent for FLAGYL) 500 mg and metformin (generic equivalent for GLUCOPHAGE)
Drug name suffix confusion is a common source of errors

**PROBLEM:** Confusion often reigns whenever a medication is available in oral dosage forms that have different release rates. The confusion multiplies when there are two or more “delayed” release formulations for the same product. We recently heard about four cases where community pharmacists dispensed METADATE ER instead of METADATE CD. ISMP also received a report where a prescription for Metadate CD 20 mg with instructions to “take two every morning” was taken to an outpatient pharmacy. It was dispensed as Metadate ER 20 mg. The patient’s mother, who worked in a doctor’s office, discovered the error after speaking with a Metadate CD drug company representative. The patient took the entire month’s prescription of Metadate ER. Both products are methylphenidate hydrochloride extended-release, but they’re not substitutable. The CD product is a once-a-day capsule with biphasic release. There’s an initial rapid release of methylphenidate, followed by a continuous-release phase, resulting in school-day-long control of attention deficit hyperactivity disorder (ADHD) symptoms. The ER product is a tablet given two to three times a day. It may be titrated to remove the need for midday dosing. The pharmacists involved in these errors weren’t aware that the Metadate CD product existed. Confusion can be expected between two other formulations of methylphenidate as well because Novartis recently began distributing another once-a-day methylphenidate, RITALIN LA. This is available along with RITALIN SR, another sustained-release dosage form.

Last year ISMP reported similar confusion between Abbott’s DEPAKOTE ER (divalproex sodium extended release) and DEPAKOTE (divalproex sodium delayed release). To make matters worse, physicians commonly prescribe extended-release products without the appropriate suffix. In an analysis of 402 prescribing errors, Lesar found that the most common type of error was failure to specify the controlled-release formulation (280 cases, 69.7%). Some products have numerous suffixes to differentiate formulations of the same drug. For example, suffixes for various diltiazem products include SR, CD, XR, XT, and a soon to be available LA formulation. In February, Biovail announced that the FDA had approved the marketing of the company’s extended-release diltiazem tablets, known as Cardizem LA. It is expected to be available this month (April 2003).

**SAFE PRACTICE RECOMMENDATIONS:** Nomenclature standards need to be established to allay confusion between various formulations of the same drug.2 Standard suffixes or

---

**Safety Briefs (cont’d from previous page)**

500 mg manufactured by Mutual Pharmaceuticals. Stock bottles of the products look very similar and could easily be confused, especially if they are stored close to one another. These particular medications can be close together whether inventory is stored alphabetically by generic name or by brand name. In this case, the inventory was stored by brand name and the drugs were separated only by one shelf. After a near miss occurred between these medications, this hazardous situation was reported internally through the chain’s Continuous Quality Improvement program, and the following recommendations were implemented in this chain’s pharmacies: (1) An alert stating “CAUTION…Make sure correct drug…METRONIDAZOLE and METFORMIN have look-alike packages” was added to the drug files for these medications in the pharmacy computer, and an override was required to proceed. (2) Signs were put on shelves near the stock bottles to alert pharmacy staff of the potential for error. (3) When new and refilled prescriptions were being reviewed, it was recommended to verify that the doses made sense and to carefully check the NDC numbers. However, this method is not foolproof. We have received error reports where the wrong drug was dispensed due to similar NDC numbers. In fact, with these two Mutual Pharmaceuticals products the first five digits and the last two digits of the NDC number are the same. Separate the products if they are close to one another on the pharmacy shelves or consider purchasing one product from a different manufacturer.

Few health professionals are aware that prescribing information for ATROVENT (ipratropium) Inhalation Aerosol states that it is contraindicated in patients with hypersensitivity to soya lecithin or related products such as soybeans and peanuts. The package label and the tear-off patient instruction sheet attached to the package insert never mention this contraindication.

cont’d on page 4
Suffix errors (cont’d from previous page)
descriptive phrases might be incorporated directly into the
drug name or a unique brand name might be needed to des-
ignate a different formulation property, as was done with
NEORAL (cyclosporine modified) and SANDIMMUNE
(cyclosporine). FDA is aware of these problems and will be
examining ways to improve trademark nomenclature.
Meanwhile, be on high alert when prescribing and dispens-
ing such medications where confusion between different for-
mulations and suffixes is likely. Build alerts into computer
systems and mark drug containers to warn staff about the
differences. After publishing the problem with various
depakote products, we heard from several readers who told
us that they designed computer mnemonics to separate the
different formulations on their screens. Store similarly
named drugs separately and use auxiliary labels to differen-
tiate the products. Keep in mind that prescriber confusion
between the various suffixes also has been reported.
Therefore, new prescriptions for any of these medications
may need to be verified. When giving or repeating back ver-
bal orders, practitioners always should use the full words
“extended release” or “sustained release,” not abbreviations.
Involving patients also may help. When prescribing and dis-
ensing one of these medications, practitioners should alert
patients to possible confusion between the various formula-
tions and suffixes.

References: 1. Lesar TS. Medication errors related to