Compounding: what was it... when, why, and what is it today?

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AFTER COMPLETING THIS ACTIVITY, PHARMACISTS SHOULD BE ABLE TO:

1. Discuss situations where compounding is appropriate
2. Describe examples of compounded products used in the treatment of various conditions where commercially available products were inappropriate for the patient.
3. Describe the difference between simple and complex compounding.

The act of combining ingredients into medicinal preparations has existed long before the term compounding. The processes of pharmacy can be dated as far back as 3000 BC; with the first documented processes of pharmacy linked back to ancient civilisations of Egypt, Rome, and Greece.

An early example is the use of the bark and leaves from the willow tree. Patients would chew on the bark or drink tea from willow tree leaves which had been brewed. The ancient Egyptians used the leaves from the willow tree to reduce inflammation of wounds and joints, to decrease pain associated with these conditions. Early pharmacists compounded the components of the herbs, flowers and trees into pastes to be applied topically or taken orally. The use of the willow bark, led to the discovery of acetyl salicylic acid (aspirin) which is derived from willow.

Over the centuries, an apothecary was a medical professional who formulated and dispensed medications to patients, physicians and surgeons. Various editions of the Australian Pharmaceutical Formulary (APF) include numerous extemporaneous preparation formulas which are referred...
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The shift back towards compounded medications has come about as awareness increased that the “one size fits all” approach of mass manufactured medications is not appropriate for all patients. The importance of pharmacogenomics has increased over the past few decades.  

In nutraceutical therapy, basic genetic and molecular profiling is conducted to map a patients’ single nucleotide polymorphisms (SNPs). This can then be used to predict a patient’s response to different medications. Physicians who follow the Walsh Protocol for nutraceutical therapy, often use genetic testing to adjust the medications to suit each patient’s biochemistry requirements. 

Today compounding, or extemporaneous dispensing, is the practice of preparing a customised medication to suit a particular patient need. In Guidelines on Compounding of Medicines, The Pharmacy Board of Australia defines compounding as “the extemporaneous preparation and supply of a single ‘unit of issue’ of a therapeutic product intended for supply for a specific patient in response to an identified need”. 

This definition of compounding is divided into Simple and Complex compounding:

- **Simple compounding** uses formulations for which information confirming quality, stability, safety, efficacy and rationality is available. This may be the preparation of formulations published in reputable sources such as the Australian Pharmaceutical Formulary and Handbook (APF). However, not all APF formulations fall under Simple compounding - for example preparations requiring to be compounded under sterile conditions.

- **Complex compounding** is the preparation and supply of a single ‘unit of issue’ of a therapeutic product that is intended for supply...
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for a specific patient, that requires or involves special competencies, equipment, processes, or facilities. Examples of complex compounded products are sterile preparations, preparations containing ingredients posing an occupational health and safety hazard such as cytotoxic or hormones, micro-dose single unit dosage forms containing less than 25 mg (or up to 25 per cent by weight or volume) of active ingredient, and sustained release or other modified-release preparations. ¹

Compounding allows patients access to treatments options, which are suited to their requirements, to facilitate improved therapeutic outcomes for patients, with a decrease in adverse effects. ²¹ For example, the commercial product (meaning the proprietary product registered or listed on the Australian Register of Therapeutic Goods) is only manufactured in dosage forms and/or strengths which are unsuitable for a specific patient; or the commercial product has been withdrawn from the market for financial reasons; or the commercial product uses excipients to which a specific patient is intolerant. This is aligned with the concept of “the right drug at the right time via the right route for the right patient.” ²²

As per Pharmacy Board of Australia’s Guidelines on compounding of medicines ³, there are three circumstances when compounding a medication may be considered:

• an appropriate commercial product is unavailable
• a commercial product is unsuitable (e.g. if a patient experienced an allergy to an excipient in the commercial product), or
• when undertaking research sanctioned by a recognised human research ethics committee.

Compounded preparations are not exempt from, and are still required to meet, the quality standards laid out in the Therapeutic Goods Act of 1989.¹ Quality assurance of all compounded preparations will need to be conducted, referring to the procedures and processes put in place by the pharmacy to ensure a high quality preparation and patient safety. As per the APF, this includes: ⁹

• appropriately-trained competent staff
• quality ingredients from approved sources
• reproducible formulations
• standard operating procedures (SOPs) for all processes involved in the compounding, including cleaning, equipment, storage, handling, documentation
• suitable equipment and facilities appropriately maintained.

When deciding to compound a medication, pharmacists are additionally required to conduct a risk assessment to determine the appropriateness of the compounded preparation for the specific patient. The Guidelines on compounding of medicines require evidence of safety, stability, and efficacy for a prescription before it is compounded, to ensure high quality patient-centred care. The patient-centred care model is also a key component of Professional Practice Standards, specifically Standard 5 and the risk management tool of Appendix 7: Compounding decision support and risk assessment tool.

In May 2018, the Pharmacy Council of New South Wales (PCNSW) released a fact sheet on “Raw materials used in compounding” which aims to provide guidance to pharmacists when sourcing the raw materials to be used in the compounding process- both active pharmaceutical ingredients (APIs) and non-active pharmaceutical ingredients.⁴ The “acceptable” materials are procured from Australian manufacturers who hold an “appropriate TGA licence to manufacture” and provide a “genuine Certificate of Analysis”. A manufacturer is defined as one involved in “any or all steps in the manufacturing process including packaging, labelling etc”. “Search Australian Manufacturers at www.ebs.tga.gov.au and/or speak to the manufacturer”.⁴

Ingredients sourced from a distributor of raw material holding solely a wholesale licence issued by a State health department do not fall in the “acceptable” category. Further information on the manufacturer is to be provided or further third party testing in Australia is to be conducted on the product. The Fact Sheet provides a Manufacturer assessment flowchart⁴ to guide raw material procurement decisions.

In addition to PCNSW’s fact sheet “Raw materials used in compounding”, pharmacists may refer to Section A of the current edition of the Australian Pharmacists' Handbook in compounding situations.
Table 1: Examples of different non-sterile compounded dosage forms. 

<table>
<thead>
<tr>
<th>State-of-matter</th>
<th>Dosage form</th>
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<tbody>
<tr>
<td><strong>Liquid</strong></td>
<td>Aromatic waters</td>
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<td></td>
<td>Foams</td>
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<td></td>
<td>Linctuses</td>
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<td>Mixtures</td>
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<td>Solutions</td>
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<td></td>
<td>Suspension</td>
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<td></td>
<td>Syrups</td>
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<tr>
<td><strong>Solid</strong></td>
<td>Suppository</td>
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<tr>
<td></td>
<td>Medication stick</td>
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<tr>
<td></td>
<td>Troche</td>
</tr>
<tr>
<td><strong>Semi-solid</strong></td>
<td>Cream</td>
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<tr>
<td></td>
<td>Paste</td>
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<tr>
<td></td>
<td>Ointment</td>
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<tr>
<td></td>
<td>Lotion</td>
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<tr>
<td></td>
<td>Shampoo</td>
</tr>
<tr>
<td><strong>Solid</strong></td>
<td>Capsule</td>
</tr>
<tr>
<td></td>
<td>Rapid dissolving tablet</td>
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</table>

Pharmaceutical Formulary and Handbook Extemporaneous. 

Risk management needs to be undertaken which involves identification, assessment, and mitigation of risk. These processes are a part of quality use of medicines to ensure high quality, safe, effective treatment options for patients, and are also required in Pharmaceuticals Society of Australia’s, Professional Practice Standards.

Compounding provides access to the preparation of various dosage forms.

**Capsules**

Capsules are solid dosage forms that can contain solids, semi solids, or liquids in a hard or soft shell. These shells are most commonly composed of gelatine, but can also be composed of cellulose, and are available in a variety of sizes which hold different volumes. The smaller the capsule size number, the larger the volume. For example, a size 0 capsule holds a larger volume (0.68 mL) than a size 3 capsule (0.3 mL). The capsule size needs to be chosen based on the volume of the powder dosage as well as the intended patient. The aim is to use the smallest volume capsule possible to fit the whole dosage prescribed, as well as the patient requirements. The most commonly compounded capsules are those that contain solids (powders). Pharmacists, and technicians working under pharmacists’ supervision, can prepare and fill compounded powder filled capsules using various methods:

1. Capsules can be filled using a capsule machine, which is the most common method of filling compounded capsules. These machines are commonly available in 100 and 300 capsule units. Partial fill kits are available which block off sections of the machine allowing a smaller number of capsules to be filled. The machine is loaded with capsules and the caps removed from the base of the capsule. The compounider then proceeds to spread and tamp the homogenously mixed powders into the capsules until all the powder is in the capsules. The capsules are then re assembled with the caps being replaced, and the capsules are locked. Amongst other quality validation procedures, a sample of the capsules should then be weighed individually to ensure even filling.

2. Capsules can also be filled by hand using the “punch” method whereby the powders are triturated and mixed by geometric dilution to form a homogenous mixture. The capsule base is then “punched” into the powder, filling the capsule until it contains the correct weight.

When compounding capsules, the compounder will find that the entire volume of the capsule will not be filled by the dosage of the prescribed API. The remaining volume will need to be filled with an excipient, often referred to as a filler. Commonly used fillers in capsule compounds include proprietary capsule filling blends, microcrystalline cellulose, lactose, hypromellose and mannitol. The filler used needs to be appropriately chosen to suit the API and the intended method of delivery. Refer to Ullmann P,
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Commonly used fillers in capsule compounds include proprietary capsule filling blends, microcrystalline cellulose, lactose, hypromellose and mannitol.

A compounder may compound a capsule when a commercial product has been removed from the market for reasons other than safety or efficacy. An example of this scenario includes the commercial product Cafergot™ (currently not available in Australia) which is a migraine treatment containing caffeine and ergotamine. A physician may prescribe a compounded version of these capsules in a case where the current commercially available migraine treatments have proven to be unsuitable for a patient.

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An example of when a compounder can prepare a dosage form when there is no commercial product available is dehydroepiandrosterone (DHEA) capsules. These capsules are compounded for patients being treated for premature ovarian failure. Currently there is no commercial product pharmaceutical (non-homeopathic) DHEA available on the Australian market.

Lactose is a commonly used filler in a variety of the commercially available capsule products. There are a number of patients who are unable to tolerate lactose due to medical conditions. Compounders may be able to compound a treatment option for these patients using a filler other than lactose that suits the API they are incorporating. There are a number of lactose-free proprietary capsule filler powder blends on the market. These were developed to enhance absorption, protect against hygroscopicity, and improve dissolution rates of the APIs.

Creams

Creams are preparations intended for application to the skin or the mucous membranes such as the vagina and the rectum. Cream bases may be compounded as either oily creams or aqueous creams. When determining which cream base to use in the preparation, the compounder considers several determinants; the physiochemical properties of the API, the physiochemical properties of the base, the intended site of application, and the intended method of delivery (topical vs transdermal).

Once a patient has tried the commercially available treatment options without sufficient relief of their symptoms, a physician may decide to treat a patient who presents with chronic anal fissures with a 2% diltiazem cream. This will need to be prepared in a cream base suitable for rectal application by a compounding pharmacy.

Another example is Bactroban™, a commonly used topical antibiotic product, which contains 2% mupirocin as mupirocin calcium. For a long period of time in 2017, this commercial product was out of stock from the manufacturer. After consultation with the physician, to determine that there were no other therapeutic treatment
Compounding of topical preparations for local or transdermal effect may reduce the risk of systemic adverse events.\(^\text{39}\)

Options for patients, compounding pharmacists were able to prepare this preparation. To confirm stock availability of commercial products, compounders are able to check the “Medicine Shortages Information Initiative” webpage on the Therapeutic Goods Administration website, or may confirm with pharmaceutical wholesalers and the manufacturers.

Compounding of topical preparations for local or transdermal effect may reduce the risk of systemic adverse events.\(^\text{39}\)

For example, patients experiencing neuropathic pain after a shingles infection may be prescribed oral gabapentin capsules for pain management. However, in some cases, the adverse reactions experienced by patients have led to the cessation of treatment. Their physician may take a topical approach to treat the neuropathic pain using compounded topical gabapentin\(^\text{24}\) in order to reduce potential gastrointestinal adverse reactions.

Veterinary patients also benefit from compounded treatment options. Cats are commonly known to suffer from hypothyroidism, however, administering oral medication can be challenging. Compounding pharmacists may prepare a transdermal methimazole 5 mg/ 0.1 mL pluronic lecithin organogel (PLO) to be applied to the pinna.\(^\text{25}\) This preparation can be dispensed in a metered dosed syringe device that accurately dispenses 0.1 mL per actuation. This facilitates convenient application to the cat’s ear and accurate dosing.

**Gels**

A gel is a semi solid preparation which consist of suspensions made up of either, small inorganic particles or large organic molecules, which are interpenetrated by a liquid.\(^\text{5}\)

Gels can be utilised in several routes of administration including oral, topical, transdermal, intranasal, vaginal and rectal.\(^\text{14}\)

Gel bases can be divided into several classifications including inorganic, organic, hydrogels, and organogels.\(^\text{14}\) The gel base chosen will depend on the route of delivery required for the API. Similarly to creams, compounders may purchase pre-made proprietary gel bases, or may compound a gel base from raw ingredients.

When would a compounding pharmacist need to prepare a gel preparation? A patient with severe chronic Achilles tendon pain, and a history of gastrointestinal (GI) issues, has tried all the available topical pain relief creams without reduction in their pain symptoms. The physician may collaborate with the compounding pharmacist in determining the treatment options. Given the patient’s history of GI issues, oral medication would not be appropriate; however, options of a compounded high-strength topical non-steroidal anti-inflammatory (NSAID) may be considered. Topical 10% diclofenac gel has been found to be efficacious for the reduction of pain associated with inflammation.\(^\text{10}\)

This is a viable treatment option for this patient offering an alternative dosage route of the NSAID which has decreased systemic side effects.\(^\text{11}\)

When a teenage patient suffering from moderate acne vulgaris has been treated with all over-the-counter commercial acne preparations without relief of their symptoms, the physician may prescribe the commercial topical clindamycin products. Where there is a need to avoid the systemic adverse events associated with the oral treatments, the use of a topical compounded treatment supported by evidence of safety, efficacy and stability, such as a topical niacinamide 4% gel, may be compounded.\(^\text{30}\)

Eosinophilic oesophagitis is a painful inflammatory condition of the oesophagus caused by inhaled or ingested allergens. Given the nature and the target site of the disease, it has proven difficult to treat with the commercially available products. Compounding pharmacists may prepare a Budesonide 1 mg/mL oral oesophageal gel using pluronic gel 20% as the base.\(^\text{32}\)

Patients are then able to swallow this preparation which will coat the oesophagus to provide relief.

Ointments and pastes are prepared for the following reasons: \(^\text{16}\)
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Oral liquids may need to be compounded in order to increase patient compliance to improve therapeutic outcomes.

- Protection of the skin from the environment
- Hydration of the skin
- Topical or systemic delivery of APIs.

A number of features determine the amount of drug that will penetrate into the skin from an ointment or paste. These include surface area, condition of the skin, pressure applied, the base used, and if an occlusive dressing is used or not. When choosing an ointment base a number of factors need to be considered. This includes drug specific factors such as stability of the API in the base, and also if the API will be bioavailable in the base chosen.

A commonly compounded ointment preparation is a salicylic acid and coal tar ointment, applied topically, for the treatment of psoriasis. The formulation for this preparation can be found in numerous editions of the APF, including the latest.

Trichloroacetic acid paste, also known as Upton’s paste, is an APF formulation used for the treatment of warts that is still compounded today. The formulation contains trichloroacetic acid 10 g, salicylic acid 60 g and glycerol 20 g. It is prepared by triturating together trichloroacetic acid and salicylic acid. Glycerol is then added until a stiff paste is formed.

Oral liquids
Oral liquids are prepared for patients who have difficulty swallowing solid dosage forms. These preparations include aromatic waters, elixirs, linctuses, mixtures, solutions, suspensions and syrups. Oral liquids may need to be compounded in order to increase patient compliance to improve therapeutic outcomes. Oral liquid preparations are susceptible to chemical, physical, and microbial instability. The characteristics of the API such as solubility in various solvents/co-solvents, pH of stability, pH of solubility, risk of hydrolysis, oxidation, and chelation, and risk of microbial proliferation need be considered. Even palatability of these preparations is an important factor to be considered, as taste affects patient compliance. Various flavours and sweeteners may be required to mask the taste characteristics of the APIs including bitter, salty, acidic, and metallic tasting drugs. A compounder can prepare an oral liquid vehicle using a proprietary base or may prepare a base themselves. There are many proprietary bases on the market including syrups, suspensions, mixes (combination of syrup and suspension), and some of which are pH buffered.

A commonly compounded oral liquid suspension is omeprazole, a proton pump inhibitor used in the treatment of Gastro-oesophageal reflux disease. Currently in Australia, there are commercially available tablets and capsules. However, the majority of paediatric patients are unable to swallow the commercially available products. When the physician decides to have a compounded oral liquid prepared for their patient, the compounder needs to assess the chemical and physical stabilities of the omeprazole when it is in a liquid dosage form. Omeprazole has a narrow pH of stability. This is an alkaline pH with a maximum pH of stability of 11 and rapid decomposition below a pH of 7.8. The formulation needs to include an alkaliniser, such as sodium hydroxide, to increase the pH. This ensures the omeprazole will be within the pH of stability range; or the compounder may use a commercially manufactured alkaline pH buffered base.

Another compounded oral liquid formulation is melatonin. This is a commonly prescribed medication used to treat insomnia and sleep disturbances in the paediatric and geriatric populations. Currently the only non-homeopathic melatonin product available on the market is an oral prolonged release 2 mg tablet (Circadin™).

A number of these patients are unable to swallow the commercial product. Compounders are able to prepare an oral suspension of melatonin to overcome the swallowing issue of these populations, with 2 mg/mL being the most commonly prepared strength.

Xerostomia, also known as dry mouth, is a condition where...
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Table 2: Relationship between the drug release, drug and base in suppositories. 12

<table>
<thead>
<tr>
<th>Drug:base characteristics</th>
<th>Approximate drug-release rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oil-soluble drug: oily base</td>
<td>Slow release; poor escaping tendency</td>
</tr>
<tr>
<td>Water-soluble drug: oily base</td>
<td>Rapid release</td>
</tr>
<tr>
<td>Oil-soluble drug: water-miscible base</td>
<td>Moderate release rate</td>
</tr>
<tr>
<td>Water-miscible drug: water-miscible base</td>
<td>Moderate release; based on diffusion; all water soluble</td>
</tr>
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</table>

patients suffer from reduced salivary flow causing a dry mouth. 27 Pilocarpine is a treatment used to increase salivary flow. 28 This is used as an oral rinse by patients who suffer from xerostomia, compounded by pharmacists, as currently there is no appropriate commercial product.

Suppositories

Suppositories are solid dosage forms used for rectal and vaginal administration of APIs for both local and systemic delivery. They may be prepared with a variety of bases including oil-soluble and water-soluble bases.

Dyspareunia (pain on sexual activity) is a condition women suffer from associated with a variety of causes, from structural to physiological, including vaginal atrophy. When DHEA pessaries are prescribed for such patients, they need be compounded 29, as currently there are no commercial DHEA pessaries available on the Australian market.

When choosing which base to compound with there is an extreme importance in examining the API characteristics with those of the base and the intended drug release rate.

Diazepam 10 mg suppositories, compounded for use during epileptic seizures, need to be prepared in a water-soluble base such as polyethylene glycol, in order to facilitate rapid release of the active from the base. The rapid release is a result of the aqueous base dissolving in the aqueous mucosal fluids of the rectum or vagina resulting in greater contact of the API with the membrane wall, making it available for absorption. 13 The ramifications of choosing an inappropriate base was demonstrated in a case in USA when a teenager was treated with 10 mg compounded diazepam suppositories, yet presented to hospital on a number of occasions with uncontrollable seizures, despite the correct use of the diazepam suppositories. The lipophilic diazepam was compounded in cocoa butter, which is a fatty acid base. The use of an oil-soluble drug in an oily base resulted in the API affinity for the base rather than the rectal fluid, low partitioning out of the base, and consequently an under-dose for the patient. 13

Troches

Troches are sub-buccal absorbed lozenges, formulated to dissolve slowly in the buccal cavity, used for both local and systemic effects. They can also be formulated to be chewed and swallowed which has benefits for paediatric and geriatric patients. 5 When used for systemic effects the preparation is able to be dosed sub-buccally, avoiding first-pass metabolism, potentially allowing a reduction in the dose of the API.

An example of when a compounder may compound a troche is when a patient presents to the pharmacy with symptoms of burning mouth syndrome. The patient has tried several topical and oral treatment options, which resulted in significant side effects. After consultation with the patient and the physician, it may be determined to compound a Clonazepam troche formulation for local effect, which has been shown to be safe and effective in the treatment of burning mouth syndrome. 18, 19 A gelatine-base troche preparation slowly dissolves in the mouth for local therapy, reducing the systemic side effects. 19

Oral progesterone is associated with a large number of adverse events. 33 In particular drowsiness, which can be caused by the potent positive allosteric modulators of GABAA receptors, due to the progesterone metabolites, for example allopregnanolone. 34 A sub-buccal troche may be compounded, which will aim to
reduce the adverse effects by reducing first pass metabolism, thereby allowing a reduction in the dose administered and potentially reducing adverse events.

Conclusion
To ensure quality use of medicines, compounding pharmacists are compelled to use multiple levels of consciousness when determining whether and how to compound a preparation for their patients. Compounding is far more than just the manual dexterity of preparing the dosage form. The most appropriate dosage form for the specific patient needs to be chosen, delivered by an appropriate delivery vehicle for the specific API required. The compounding is to be conducted by appropriately trained staff, following SOPs in appropriate facilities, using appropriate equipment and the highest quality ingredients on the market. Risk management includes making the decision not to compound if the identified and assessed risks in the given compounding conditions cannot be adequately mitigated.

Compounding today allows the preparation of customised pharmaceutical treatment options for patients. Compounding pharmacists are able to change the route of delivery of medications, change the dosage form for the same route of delivery, remove allergens, and prepare medications that are not commercially available. This flexibility increases the treatment options available to clinicians in the treatment of patients, with the underlying aim being to improve therapeutic outcomes.

References


35. GOLDBERG D. Aspirin: Turn-of-the-Century Miracle Drug. Distillations. 2009;.


1. Which of the following circumstances is compounding suitable?

A. The commercial product comes in a 2mg capsule whereas the patient’s dose is 4mg  
B. The patient is unable to afford the commercial product  
C. The patient has an allergy to the colour in the commercial product.  
D. The commercial product was removed from the market for safety concerns

2. The aims of compounding a medication for a patient include:

A. Improving patient compliance by reducing side effects  
B. Eliminating risk of allergy  
C. Improving therapeutic outcomes for patients  
D. Increasing therapeutic treatment options  
E. All of the above

3. Which of the following controls support the quality of compounded preparations?

A. Sourcing raw ingredients from TGA-approved manufacturers  
B. Implementing Standard Operating Procedures  
C. Following formulas which are published in reputable sources  
D. All staff involved undergoing competency-assessed training  
E. All of the above

4. All medications supplied to patients, both compounded and commercially available, are required to meet standards of efficacy, safety, and stability.

A. True  
B. False

5. Which of the following statements regarding compounding is INCORRECT?

A. Simple compounding uses formulations for which information confirming quality, stability, safety, efficacy and rationality is available.  
B. Complex compounding is the preparation and supply of a single ‘unit of issue’ of a therapeutic product that is intended for supply for a specific patient, that requires or involves special competencies, equipment, processes or facilities  
C. All APF formulations are classed as simple compounding  
D. Sterile preparations are examples of complex compounding  
E. Preparations containing ingredients posing an occupational health and safety hazard are classed as complex compounding.
6. Which of the following statements regarding capsules is CORRECT?

A. All capsule shells are composed of Gelatine
B. The smaller the capsule size number, the smaller the volume it contains.
C. Commonly used capsule fillers include microcrystalline cellulose, lactose, hypromellose, and mannitol
D. A compounder may compound a capsule when a commercial product has been removed from the market for safety reasons
E. ALL of the above

7. Which of the following statements regarding compounded oral liquids is INCORRECT?

A. Oral liquids are prepared for patients who have difficulty swallowing solid dosage forms.
B. Compounders should only prepare an oral liquid vehicle bases themselves.
C. Oral liquid preparations include aromatic waters, linctuses, mixtures, suspensions, and syrups.
D. Oral liquids are susceptible to chemical, physical, and microbial instability.
E. Various flavours and sweeteners may be required to mask the taste of some APIs.

8. Which of the following statements regarding compounding suppositories is CORRECT?

A. An oil-soluble drug compounded into an oily base will produce a suppository with a moderate release rate.
B. An oil-soluble drug compounded into a water-miscible base will produce a suppository with a slow release rate.
C. A water-miscible drug compounded into a water-miscible base will produce a suppository of extremely slow release.
D. A water-soluble drug compounded into an oily base will produce a suppository with a rapid release rate.
E. ALL of the above.