INTRODUCTION
In recent years, there has been a growing interest in the subject of the care of individuals at the end of their lives. The aging population is growing at an increasing rate owing to postwar demographic trends and advances in medical treatment. Individuals want to live as long as possible, but also want to be free from the indignities of advanced age and to continue to live as a young person. It appears there must be a certain quality of life in old age or else a quick death.

BACKGROUND
In the past century, the experience of dying has been transformed from a part of daily life to a highly technological event. Before the use of antibiotics and modern medicine, people died at a younger age and with less forewarning. Healthcare practitioners could do little but visit and attend to the dying by helping to relieve some of their suffering. Today however, with all the great advances in modern medicine, many diseases are diagnosed early; with new technology and pharmaceutical agents, patients may live for an extended period of time before dying. Post WWII individuals were often sent to hospitals or institutions to die. Today, we know that many prefer to spend their last days at home with family.

The hospice movement was actually established in the 11th century by the Crusaders. They established places where travelers going to and returning from the Holy Land were cared for and refreshed, the sick and dying were also admitted and cared for. The Knights Hospitallers of St. John of Jerusalem, founded a “way station” in Jerusalem for sick and weary pilgrims that was extended to Tyre, Acre and eventually to Cyprus. The Hospitallers were recognized by the Pope as a military order in 1113 and they can be traced throughout history. The Irish Sisters of Charity founded Our Lady’s Hospice for care of the dying in Dublin prior to 1900. Hospice came to North America in 1971 where it began in New Haven, Connecticut, and a home care service began there in 1973. The hospice movement began to spread throughout the US in the mid-1970s. It is estimated that there are now approximately 2,900 hospices in the US serving about 450,000 patients; there has also been considerable growth in European hospices since the fall of Soviet Communism.

DEFINITIONS
“Hospice” is a term that is not very clear and has different meanings to different people. Some believe hospice is a place to die, some associate it with the word “death” and some think of it as a place of providing both competent and compassionate care; care provided to people facing death by people unafraid to face death.

Hospice can be an ambiguous word, which offers some advantages. It often allows us the opportunity of explaining what we mean. It can be said that it is a metaphorical term, alluding to death indirectly through the comparison of a “way station” on life’s last journey. Hospice patients include mostly the elderly, but also encompasses individuals of all ages; there are now hospices that specialize in the care of the dying child. Hospice comes from the Latin word Hospitium, meaning hospitality, and from the old French word Hospes, or host. In dictionaries, one may read of a definition of hospice as a shelter or lodging for travelers, children, or the destitute, often maintained by a monastic order. Today, the word hospice is used to describe a program of care for individuals and their families facing a terminal illness. The National Hospice Organization (NHO) defines hospice as: “a coordinated program providing palliative care to terminally ill patients and supportive services to patients, their

GOALS AND OBJECTIVES
Goal: To provide compounding pharmacists supportive information on compounding for the hospice patient along with specific formulas for the treatment of patient symptoms.

Objectives: After reading and studying the article, the reader will be able to:
1. discuss the purpose of hospice care.
2. describe the rationale for hospice care and the focus of treatment.
3. list the primary symptoms experienced by the terminally ill hospice patient.
4. recommend specific formulations that might be of benefit in treating the symptoms experienced by hospice patients.

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families, and significant others 24 hours a day, seven days a week. Comprehensive/case managed services based on physical, social, spiritual, and emotional needs are provided during the last stages of illness, during the dying process, and during bereavement by a medically directed interdisciplinary team consisting of patients/families, health care professionals and volunteers. Professional management and continuity of care is maintained across multiple settings including homes, hospitals, long term care and residential settings.” (NHO, 1993).

NATIONAL HOSPICE ORGANIZATION
The NHO was founded in 1978 during which 1,200 hospices were listed in the directory. The U.S. hospice movement was distinctly oriented toward home care, as most Americans surveyed showed a preference for dying in their homes.

Some characteristics of U.S. hospice care are evident and include the following:

- The patient and family are the unit of care.
- Care is provided either in the home or in inpatient facilities.
- Services are available on a 24 hours a day, 7 days a week basis.
- Hospice care is interdisciplinary.
- Hospice treats the whole person.
- Symptom management is the focus of treatment.
- Pharmacists play a major role in hospice care as relief of symptoms generally requires pharmaceuticals.

Hospice care focuses on the physical comfort of its patients. Control of symptoms is paramount and includes control of pain, nausea/vomiting and bowel function, maintaining an alert mind, intact skin and the relief of breathlessness.

WORKING WITH HOSPICE PATIENTS
Dying generally involves the loss of being a healthy person, of being able to work, of being with friends, of being able to care for oneself, of a future, etc. Each individual handles these aspects of life in their own way.

In working with hospice patients, one must always remember that the patient sets the agenda. Hospice workers cannot impose their ideas and wishes or force the person to respond. Working with the dying demands great tolerance and patience.

Hospice patients usually fear the dying process more than death itself. Dying is often equated with suffering; to face death often means one must face inescapable suffering. Hospice care assists in minimizing suffering during dying. Today, nearly all hospice patients are free of physical pain in the time leading up to their deaths. There is a point in the care of a hospice patient where the focus of care shifts to the goal of comfort, and no longer healing. That focus is not to fight for a cure but to simply live as fully as possible for as long as possible; to do this, the patient must be relieved of distress.

SYMPTOM MANAGEMENT
Care of the hospice patient generally centers around symptom management and helping the patient to be more comfortable. The following questions can be considered in evaluating the nature and severity of symptoms experienced by the patient.

1. How do the symptoms affect the patient’s life?
2. How do the symptoms affect the patient’s physical function and mobility?
3. What makes the symptoms better (i.e.; position, activity, medicine, food)?
4. What makes the symptoms worse?
5. Are the symptoms worse at any particular time of day or night?

The most common symptoms experienced by patients include pain, nausea/vomiting, dyspnea, constipation, diarrhea, hiccups, anorexia, cachexia, anxiety, confusion, asthenia, oral hygiene problems, decubitus ulcers and symptoms associated with impending death.

Pain
Generally, the first symptom to relieve distress is associated with pain. Pain is what the patient says is pain. It is subjective, multidimensional and can include psychological, social and spiritual aspects. Pain can be either chronic or acute; generally the pain becomes chronic in nature.

Proper control of pain requires an assessment of the type of pain that the patient experiences. There are many different pharmacological agents that can be used to treat different types of pain; somatic, visceral and deafferentation pain.

Pain medication must generally be given around the clock. It is generally given in anticipation of pain, not necessarily in response to pain. The patient must have flexibility in dosing so that a baseline level of pain relief is obtained with the opportunity of immediately addressing “breakthrough” pain. In many cases, long-acting products are used where the proper dosage is determined by titrating the patient and allowing the patient to use immediate acting products for “breakthrough” pain. If the use of the immediate release products becomes more frequent, the dose of the long acting products is usually increased. Also, one must learn that there is usually no such thing as an “overdose”. The dose of the analgescics used should relieve the pain and not cause sedation and side effects.

Generally, the patient is asked to rate their pain on a scale of 0 through 10, where 0 is being free of pain and 10 is the worst imaginable pain. Although most patients would prefer to be free of pain, many are quite content with maintaining the pain at about 3 or below on this scale.

Nausea/Vomiting
Nausea and vomiting occur in a reported 60% of terminal cancer patients, but these symptoms tend to be intermittent. Nausea can be due to drug side effects, oral thrush, brain metastases, anxiety, gastric irritation, intestinal obstruction, constipation, small stomach syndrome, hypercalcemia, uremia and a low-grade urinary tract or pulmonary infection. It usually has more than one cause. Appropriate routes of administration of antinauseants include parenteral, rectal and transdermal.

Drug therapy has included neuroleptics (haloperidol, prochlorperazine), antihistamines (cyclobenzaprine, dimenhydrinate), anticholinergics (hyoscine), prokinetics (metoclopramide, domperidone, cisapride), 5HT3 antagonists (ondansetron, granisetron), corticosteroids (dexamethasone) and benzodiazepines.

Dyspnea
The incidence of dyspnea in advanced malignancies can range from 48-79% in patients. It is a frequent part of the dying process and can be due to multiple causes, including anemia, ascites, bronchospasm, cardiac failure, lung collapse, lung infection, pericardial effusion, pleural effusion, pneumothorax, pulmonary emboli and superior vena cava obstruction. The treatment varies depending upon the etiology and the condition of the patient, but can include bronchodilators, corticosteroids, sedatives and oxygen.

Constipation
Constipation is a frequent complaint and may be related to the use of narcotics for pain management. In addition to drug use (narcotics, diuretics, anticholinergics, aluminum-containing antacids), other causes of constipation include a low-fiber diet, failure to heed the urge (due to lack of privacy or incorrect positioning) or reduced defecation (possibly due to anal fissure or hemorrhoids), dehydration, depression and hypercalcemia. Generally, patients should go no more than three days without a bowel movement. Laxative treatment should include both a
fetal softener and a stimulant laxative. Generally, bulk-type laxatives should not be used as they may lead to impaction.

**Diarrhea**

Causes of diarrhea may include steatorrhea (due to malabsorption of fat), malignant intestinal obstruction, laxative imbalance, rectal tumor, fecal incontinence due to lack of sphincter control and a carcinoma tumor.

**Hiccups**

Hiccups are a reflex that results from irritation of the vagus nerve or by stimuli from other parts of the central nervous system. The reflex is processed in the brain stem and is inhibited by increased carbon dioxide in the blood and by stimuli from the pharynx. It can be caused by irritation of the vagus nerve, irritation of the phrenic nerve and by the central nervous system. Drug therapy can be implemented with an antacid preparation with dimethicone; every 4-6 hours. If not effective, metoclopramide (10-20 mg every 4-6 hours) or cisapride (20 mg every 12 hours) can be added. If it persists, baclofen (5-10 mg every 6-12 hours) can be substituted for the metoclopramide. The rationale is that the antiflatulent drugs facilitate belching, reducing gastric distension; metoclopramide hastens gastric emptying, and baclofen relaxes the diaphragm. Other drugs that have been used include chlorpromazine, haloperidol, phenytoin, sodium valproate, carbamazepine and nifedipine.

**Anorexia**

The majority of hospice patients experience a loss of appetite (anorexia) as their illness progresses. Taste abnormalities are relatively common in seriously ill patients and the body needs less intake when it is inactive. Some causes are reversible, but progressive anorexia is a natural part of dying. Other factors that may contribute include chemotherapy, radiation therapy, oral thrush, constipation, nausea, hyponatremia, hypercalcemia, chemotherapy and depression. Corticosteroids have been used to increase appetite.

**Cachexia**

The extent of muscle wasting and weight loss during cachexia is much greater than would be expected simply from reduced food intake alone. Also, cachexia is not reversed by increased food intake. Causes of cachexia include vomiting, diarrhea, malabsorption, reduced food intake, hemorrhage, ulceration, increased metabolic rate, abnormal metabolism, surgery, chemotherapy, radiation therapy, starvation and diabetes mellitus. Therapy has included corticosteroids, progestogens, prokinetic drugs (metoclopramide) and parenteral and enteral nutrition.

**Anxiety**

Anxiety is a normal reaction in most patients; however, some patients have a severe and prolonged reaction to the physical effects of the illness and its potential implications for the future. The realization that death is approaching may cause feelings of regret, missed opportunities and guilt and fear of suffering of what happens after death. Causes can be fear of the illness/treatment, thoughts about the past/future, worries about family/finances, incomplete or conflicting information from healthcare workers/family, loss of independence, pain, dyspnea, nausea, weakness, drugs (neuroleptics, stimulants, corticosteroids), drug withdrawal (alcohol, benzodiazepines), depression, delirium and paranoia. Drug therapy has included antidepressants, benzodiazepines, antipsychotics and propranolol.

**Confusion**

About 30% of cancer patients will experience confusion at some point during their illness which may be a result of drugs, full bladder, pain, impaction, brain metastases, infection, metabolic imbalance, anxiety, withdrawal from alcohol or benzodiazepines and delirium. Many drugs, including psychoactive drugs, diuretics, beta blockers, anti-Parkinsonism drugs and sulfonamides can also cause confusion.

**Asthenia**

The loss of energy, generalized weakness and rapid tiring during exercise are common symptoms of terminal illness and may be a part of the anorexia-cachexia syndrome. It may result from illness (anorexia, inactivity, anemia, hyponatremia, hypoadrenalism, renal/liver failure), be cancer-related, treatment related (surgery, chemotherapy, radiation therapy, drugs-diuretics, antihypertensives or oral hypoglycemics), or result from infection, dehydration, malnutrition and starvation. Drug therapy for asthenia is limited but has included corticosteroids and progestogens.

**Oral Hygiene**

Routine oral hygiene can prevent discomfort, facilitate eating/drinking, prevent halitosis, minimize social isolation and psychological distress; ensure that the oral mucosa and lips are moist, clean and healthy, and remove debris and plaque from the teeth/gums.

Toothbrushes and dental floss (if practical) should be used at least twice daily. A mouthwash can be used every two to four hours. Petroleum jelly will help prevent dry, cracked lips and should be applied regularly in a thin layer at least twice daily.

Dry mouth can be relieved by drinking fluids, chewing gum, taking pilocarpine, using artificial saliva and using non-alcoholic mouthwashes. Candidiasis can be treated using a nystatin mouthwash or by taking oral ketoconazole or fluconazole.

Aphthous ulcers are painful and can be treated using tetracycline suspension mouthwash (250 mg in 10-20 mL of water in mouth for three minutes then expectorated; repeat every eight hours for three days), chlorhexidine gluconate mouthwash (0.2%; rinse with 10 mL every eight hours) and hydrocortisone lozenges (2.5 mg every eight hours). Local analgesic agents can be provided as needed.

**Decubitus Ulcers**

Pressure on the skin and tissues in contact with a chair, bed or other surface can result in decubitus ulcers. When healthy, we minimize the pressure by changing position; in the immobile patient however, damage can develop in a matter of a few hours. The earliest sign is redness (blanching erythema), followed by non-blanching erythema, partial-thickness skin loss, and then an established ulcer (a deep crater with full-thickness skin loss and damage to subcutaneous tissue).

A number of different compounded medications are commonly used for treating decubitus ulcers including such drugs as topical protectants, phenytoin and misoprostol.

**Impending Death**

Symptoms of impending death usually include a lowered body temperature, increased somnolence, confusion, incontinence, congestion in the lungs or throat, restlessness, withdrawal or detachment from others, vision-like experiences, decreased intake of fluid and foods, decreased urine output and changes in breathing.

**PHARMACIST INVOLVEMENT IN HOSPICE**

Caregivers are usually faced with the following types of procedures or conditions, some of which can be taught or alleviated by the hospice pharmacist: medication administration, catheter care, bleeding management, dressing changes, colostomy care, constipation, approaching death care, dehydration, diarrhea, elevated temperature, infection control, durable medical equipment operation, hospital bed change, body mechanisms to avoid injury, intravenous therapy, mouth care, nausea, oral and nasopharyngeal suction, oxygen safety, relaxation, seizure precautions, skin care, tracheostomy care and pain management. Hospice care is one of the most challenging parts of pharmacy practice. It must function as a noble expression of humanity and sincerity, but yet must be run as a business so care can also be provided to others. News media stories often result when the “business” side of hospice overshadows the “patient” side; to complicate matters more, government is in the picture now and seems intent on addressing primarily the “business” aspects of hospice care. Hospice care has now become managed care; if the providers spend less than they collect, they
make a profit. If they spend more than they collect, they experience a loss. The question of how to balance adequate and sympathetic patient care with the business/government aspects remains a challenge.

NOTES RECEIVED BY HOSPICE COMPOUNDING PHARMACISTS

Pharmacists routinely receive accolades from family and friends of hospice patients; this is what makes this type of practice so meaningful. The following are a few comments received by hospice compounding pharmacists:

◆ “Mom could never have experienced the peace of dying comfortably at home with the family without the medications, care and concern you provided”

◆ “I don’t know how we could have done it without the effort and work you put into making Dad more comfortable during his last week with us. Thank you, we will never forget what you did for us”.

◆ “We thank you and all at your pharmacy with all our hearts for taking care of Granddad. It seems like you are a part of our family”.

SUMMARY

Being a compounding pharmacist working with hospice patients is often difficult, requiring a creative approach to medication administration and broadening the boundaries of treatment guidelines. Also, one must be willing to try new methods and approaches as there may not be any documentation of “safety and effectiveness” for what needs to be done for the hospice patient.

In summary, it has been said that when we complete a race, we don’t just automatically stop right at the finish line. Generally, we tend to go just a little further and listen to the kind voices of family and friends; then we say to ourself, “it is finished, my work is done”. Compounding pharmacists help hospice patients cross the finish line in a more dignified and near symptom-free manner.

USEFUL FORMULATIONS FOR TREATING PAIN

Rx   Morphine Sulfate Slow-Release Suppositories

**USEFUL FORMULATIONS FOR TREATING PAIN**

M. ft. Supp. No. 1

Witepsol H-15                                qs
Alginic acid             25%
Morphine sulfate         25 to 50 mg
M. ft. Supp. No. 1

Pass the alginic acid through a #200 mesh sieve. Melt the Witepsol H-15 suppository base in a glass beaker. Sprinkle the alginic acid on the Witepsol H-15 base and mix. Sprinkle the morphine sulfate on the mixture and stir until mixed. Place the mixture on an ultrasonic bath for 10 minutes, then add the flavor and mix. Pour into molds (at room temperature) and allow to cool at room temperature. Note: molds can be prelubricated with a vegetable oil spray if necessary.

Mix the lorazepam, diphenhydramine HCl and haloperidol powders together. Prepare the hard troche base according to the formula below. After removing the hard troche base from the heat, allow it to cool for a few minutes. Sprinkle the powder on the melt with thorough mixing. Add the flavor and optional color and thoroughly mix. Pour into molds (at room temperature) and allow to cool at room temperature. Note: molds can be prelubricated with a vegetable oil spray if necessary.

Mix the lorazepam, diphenhydramine HCl and haloperidol powders together. Prepare the hard troche base according to the formula below. After removing the hard troche base from the heat, allow it to cool for a few minutes. Sprinkle the powder on the melt with thorough mixing. Add the flavor and optional color and thoroughly mix. Pour into molds (at room temperature) and allow to cool at room temperature. Note: molds can be prelubricated with a vegetable oil spray if necessary.

Rx   Troche Base

**USEFUL FORMULATIONS FOR TREATING NAUSEA/VOMITING**

Mix the lorazepam, diphenhydramine HCl and haloperidol powders together. Prepare the hard troche base according to the formula below. After removing the hard troche base from the heat, allow it to cool for a few minutes. Sprinkle the powder on the melt with thorough mixing. Add the flavor and optional color and thoroughly mix. Pour into molds (at room temperature) and allow to cool at room temperature. Note: molds can be prelubricated with a vegetable oil spray if necessary.

Mix the lorazepam, diphenhydramine HCl and haloperidol powders together. Prepare the hard troche base according to the formula below. After removing the hard troche base from the heat, allow it to cool for a few minutes. Sprinkle the powder on the melt with thorough mixing. Add the flavor and optional color and thoroughly mix. Pour into molds (at room temperature) and allow to cool at room temperature. Note: molds can be prelubricated with a vegetable oil spray if necessary.
Rx Scopolamine Hydrobromide 0.25 mg/0.1 mL Topical PLO Gel

Scopolamine hydrobromide 250 mg
Soy lecithin/Isopropyl palmitate solution 24 mL
pH 5.0 buffer solution 2.5 mL
Pluronic F127 20% gel qs 100 mL

Dissolve the scopolamine hydrobromide in the pH 5.0 buffer solution. Add the soy lecithin/isopropyl palmitate solution and mix well. Add sufficient 20% Pluronic F127 gel to make 100 mL and mix well. Package and label. Note: The pH 5.0 buffer solution can be prepared by mixing 0.1 M citric acid in purified water with 0.2 M disodium phosphate in purified water in a ratio of about 1:1. The ratio can be varied to achieve the pH 5.0 level (0.1 M citric acid contains 19.2 grams of anhydrous citric acid in 100 mL of solution; a solution of 0.2 M disodium phosphate contains 53.61 g Na2HPO4.7H2O, or 28.39 g anhydrous disodium phosphate in 100 mL of solution). The soy lecithin/isopropyl palmitate solution can be prepared by dissolving 83 g of soy lecithin granules in 100 mL of isopropyl palmitate containing 220 mg of sorbic acid and stirring with the aid of heat until dissolved.

Rx Antiemetic Suppositories of the Gralla Type

Polyethylne glycol base qs 2 g
Fatty acid base qs 2 g 2 g 2 g 2 g 2 g 2 g
Silicon dioxide 20 30 20 15 - -
Promethazine HCl - - - 10 10 5
Dexamethasone - - - - - -
Lorazepam - - - - - -
Diazepam - - - - - -
Diphenhydramine HCI - - - - - -
Phenytoin 2.5 g
Hydroxyethylcellulose 2 g
Methylparaben 200 mg
Glycerin 10 mL
Parabens qs 100 mL
Purified water qs 100 mL

Note: Quantities are given in milligrams unless otherwise noted.

Mix the powders uniformly. (Pulverize the tablets if used or empty the contents of commercial capsules). Melt the fatty acid base of the polyethylene glycol base to the suggested temperature, depending upon the specific product used. Slowly add the powders with continued stirring until uniformly mixed. Pour into the molds (maintained at room temperature) slowly and smoothly with intermittent stirring of the melt to ensure the powders remain well mixed. Allow suppositories to solidify. Package and label.

Rx Dexamethasone, Lorazepam, Haloperidol, Diphenhydramine Hydrochloride and Metoclopramide Hydrochloride in PLO Gel

Dexamethasone 1.2 g
Lorazepam 100 mg
Haloperidol 100 mg
Diphenhydramine HCl 2.4 g
Metoclopramide HCl 2.4 g
Ethoxy diglycol 15 mL
Lecithin/Isopropyl palmitate 22 mL
Pluronic F127 30% gel qs 100 mL

Blend the powders together, reducing particle size if necessary. Incorporate the powders into the ethoxy diglycol to form a slurry. Add the lecithin/isopropyl palmitate and mix well. Add sufficient Pluronic F127 30% gel to volume and mix using a shear mixing technique. Package and label.

Note: The lecithin isopropyl palmitate solution can be prepared by mixing 0.2 g sorbic acid and 50 g of soy lecithin and 50 g of isopropyl palmitate. The Pluronic F127 solution can be prepared by mixing 0.2 g sorbic acid, 30 g of Pluronic F127 and sufficient purified water to make 100 mL.

Rx Ondansetron Hydrochloride 8 mg/ mL in Pluronic/Lecithin Organogel

Ondansetron hydrochloride 800 mg
Purified water 20 mL
Lecithin/Isopropyl palmitate 22 mL
Pluronic F127 30% gel qs 100 mL

Thoroughly pulverize 100 of the 8 mg ondansetron hydrochloride tablets to a very fine powder. Add the purified water to form a slurry. Incorporate about 50 mL of the Pluronic F127 30% gel and mix well. Add the lecithin/isopropyl palmitate mixture and mix. Add sufficient Pluronic F127 30% gel to volume and mix well using a high shear technique. Package and label.

USEFUL FORMULATIONS FOR TREATING DECUBITUS ULCERS

Rx Decubitus Ulcer Gel

Lidocaine hydrochloride 2 g
Misoprostol 200 µg tablets #15
Phenytoin 2.5 g
Hydroxyethylcellulose 2 g
Methylparaben 200 mg
Glycerin 10 mL
Parabens qs 100 mL
Purified water qs 100 mL

Obtain the tablets of misoprostol and pulverize them to a fine powder; blend in the remaining powders. Add the glycerin and make a smooth paste. Slowly incorporate sufficient pure water to volume with mixing. Package and label.

USEFUL FORMULATIONS FOR TREATING ORAL SORES

Rx Misoprostol 0.0024% Mouth Rinse for Oral Ulcerations

Misoprostol 200 µg tablets #12
Methylparaben 200 mg
Glycerin 10 mL
Cherry flavor, anhydrous 10 µL
Syrup 40 mL
Sodium carboxymethylcellulose 0.25% solution qs 100 mL

Obtain the misoprostol tablets and pulverize them to a fine powder. Add the glycerin to form a paste and add the methylparaben and the glycerin and the cherry flavor. Add the syrup and sufficient sodium carboxymethylcellulose 0.25% solution to volume and mix well. Package and label.

REFERENCES


SUGGESTED READINGS

When swallowing a tablet is a problem...

A Spoonful from Paddock Helps the Medicine Go Down

The Paddock Solid-to-Liquid Solution
Documented stabilities for over 50 formulations using Ora-Plus®, Ora-Sweet®, and Ora-Sweet SF™ provide you with an extra measure of confidence to help the medicine go down.

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Free compounding assistance available from Paddock Laboratories. For additional product information, please call 1-800-328-5113 or visit www.paddocklabs.com
INTRODUCTION
In the year 2000, an estimated 20 million women will become menopausal in the United States.\(^1\) In the lives of many women, this is a life-changing event leading to requests for assistance, understanding, a sympathetic ear and treatment for some of the symptoms associated with this change.

The routine prescription for conjugated equine estrogens and medroxyprogesterone acetate fails to take the individual needs, backgrounds and lifestyles into consideration.\(^2\) In many cases, women are offered a standard brand, one-size-fits-all therapy when medical care is sought for both the physical and emotional symptoms associated with these hormonal changes occurring in the woman’s body. With managed care restraints on the time health practitioners can spend with patients, these women are not receiving the care they need and to which they are entitled. With more prescriptions being written for Premarin than for any other medication in the United States, the market is obviously present for hormone replacement therapy. This is also supported by the recent activities among pharmaceutical companies to market their own brands of conjugated estrogens.

Individualization of patient care rather than mass treatment is one issue here. The question is, what degree of individualization of care is really needed? What can be provided? Who can provide it? Another question to answer is whose decision is it...the patient’s, her health care provider’s or the third-party payer’s?

As the baby boomers (born during WW II) move into mature adulthood, this area will no doubt continue to increase in importance. We are presenting this issue for the support of quality compounding of natural hormone replacement preparations.

DEFINITIONS AND ABBREVIATIONS
ERT is estrogen replacement therapy and involves treatment using a number of different estrogens that are available. HRT is hormone replacement therapy and involves a combination of hormones, including estrogens, progestins and even androgens.

Natural (bio-identical) hormones refer to those hormones that are molecularly identical to those made in the human body and have the same exact chemical structure.

Plant-derived refers to those hormones that are chemically derived from precursors found in yam or soy plants. Chemically, they will have the same chemical structure as those that are totally synthesized.

Synthetic (Patented, Conventional, Artificial) hormones are those that are not usually found in humans and are chemically different from the naturally occurring human hormones. They are not identical in structure or activity to the natural hormones they are designed to emulate.

The Natural Hormones include estrone (E1), estradiol (E2), estriol (E3), progesterone, testosterone, dehydroepiandrosterone, pregnenolone and androstenedione. In humans, the estrogens are primarily composed of 10-20% estradiol (E2), 10-20% estrone (E1), and 60-80% estriol (E3). For comparison, Premarin\(^{\circledast}\) is composed of 5-19% estradiol (& others), 75-80% estrone and 6-15% equilin.

THE MENSTRUAL CYCLE
In a woman’s life, between puberty and menopause, the menstrual cycle is somewhat regular and predictable and can be divided into about 7 phases, each lasting the approximate number of days as indicated in Table 1. During the different phases of the cycle, there is a constant changing of the quantity of estrogens, progesterone, LH and FSH in the body.

The estrogens are responsible for normal growth and development of female sex organs, maintenance of secondary sex characteristics, promoting the proliferation and growth of specific cells in the body, protection against bone loss and protection against heart disease.

Progesterone (1) is important for promoting secretory changes in uterine endometrium (counteracting the prolific action of the estrogens), (2) is necessary for maintaining pregnancy (maintains the uterine lining and decreases uterine contractions), (3) prepares the breasts for lactation, stimulates osteoblast-mediated new bone formation (increases bone mass and density) and, (4) is metabolized to other active hormones.

Testosterone serves to enhance libido, provides cardiovascular protection (lowers cholesterol), enhances bone building (increases calcium retention) and improves the energy level and mental alertness.

Estrogens, progestins and androgens are important endogenous hormones that produce numerous physiological actions. Their
As one emerges from childhood to adolescence, these hormones are responsible for many of the physiological changes that occur to prepare one for adulthood. Throughout one’s adult life, these hormones are usually kept in balance but may be modified through the administration of additional hormones, as in the case of contraception. Nonetheless, adult life is generally characterized by the presence of circulating levels of these hormones.

As one continues to mature into the fifth decade or so of life, these hormones generally start decreasing in prevalence and changes in the adult body begin to occur to prepare one for mature adulthood. These changes generally involve a decrease in these hormones leading through a change in life termed the menopause. While most think of menopause as related to women, there are also changes in the male at about the same time in life.

The symptomatology associated with these changes is uncomfortable for many patients and they seek medical help. Since the hormones the body has been producing and responding to generally involve estradiol, estril, estrone, progesterone and testosterone, these are termed “natural” and their replacement is termed “natural hormone replacement therapy”. This is compared to the administration of other estrogens, progestins and androgens that are commercially available that are chemically modified products, even though they may actually come from natural animal (nonhuman) sources. As the natural hormones are not patentable substances, there has been little historical interest from the pharmaceutical industry in promoting their use. However, as compounding pharmacists, this provides opportunities for meeting patient needs on an individual basis.

THE STAGES OF A WOMAN’S LIFE
A woman’s life can be divided into four different stages as it relates to menopause.

1. Premenopause occurs at the onset of the first menstrual period and is characterized by routine fluctuations of estrogens, progesterone, luteinizing hormone and follicle stimulating hormone.
2. Perimenopause occurs between the onset of changes in the hormonal secretions and the onset of menopause. There are fluctuating hormonal secretions due to intermixed normal and abnormal menstrual cycles. This is also called the period of estrogen dominance.
3. Menopause occurs at the termination of the menstrual periods and is defined as missing twelve consecutive periods. It should be noted that not all women experience problems associated with menopause.
4. Postmenopause is the period of time following the last menstruation. During this time, HRT can be used to aid in heart protection, improve the lipid profile and enhance bone mass.

SIGNS AND SYMPTOMS OF MENOPAUSE
The reduction of endogenous estrogens and progestogens after menopause results in a variety of vasomotor symptoms in women. These often experienced signs and symptoms of menopause are listed in Table 2 (Symptoms associated with a decrease in estrogen) and Table 3 (Symptoms associated with a decrease in progesterone). Menopause is not an illness, but a natural occurrence in a woman’s life that may lead to increased risks, including heart disease, specifically, myocardial infarction and angina. Osteoporosis is another major health problem as well as vaginal atrophy and Alzheimer’s disease.

TREATMENT
The treatment of menopause is, to some degree, seeking an elusive answer to hormone imbalance. The patient and health care provider is, in many cases, seeking a simple answer to a complex problem, or set of symptoms. One simple answer generally does not exist. A few general rules can be stated related to hormone replacement therapy.

1. There is no simple answer or single approach to HRT.
2. Treat each patient as an individual.
3. HRT may be difficult and is time consuming.
4. Generally, one cannot successfully treat hormone imbalances with hormones alone.

The decision to use HRT is an individual one, based on the individual’s particular risks. The goals of natural HRT are to (1) alleviate the symptoms caused by the natural decrease in production of hormones by the body, (2) replace the hormones to the extent to provide positive benefits, (3) bring the body back to normal hormonal balance, and (4) imitate the body’s natural processes as much as possible.

The natural aging process results in a decrease in selected hormone levels in the body. These natural hormones are made by the body and have contributed to survival and longevity throughout the life span of the human race. These hormones are not dangerous and have not subjected women to disease and it is not likely that we will develop a better synthetic drug to take their place. Consequently, it only makes sense to provide back to the body the exact chemical hormones to replace the lower levels that occur as a result of menopause.

The benefits of natural HRT include (1) minimizing symptoms of menopause prevention of osteoporosis, (2) improved lipid profiles, (3) reduced risk of heart disease, (4) reduced risk of endometrial and breast cancer, and (5) prevention of Alzheimer’s disease.

HORMONES AND DOSING
Postmenopausal dosing guidelines vary with the patient and what is presented is only a guide. Each patient must be individually assessed, dosed and followed. Dosing of Double Estrogens or Triple Estrogens is generally in the range of 0.625 to 5 mg given once or twice daily. Progesterone is usually dosed in the range of 25 to 200 mg daily. Testosterone is often dosed in the range of 0.25 to 2 mg daily. Obviously, these doses can be lowered or raised based upon the response of the patient and the dosage form that is used. The Double Estrogen mixture consists of 80% estril and 20% estradiol. The Triple Estrogen mixture consists of 80% estril, 10% estrone and 10% estradiol.

Various routes of administration are used, including oral, transdermal, nasal, vaginal, sublingual, buccal and others. In the oral administration of capsules, the release rate of the hormone is often retarded by the use of a cellulose polymer that forms a gel when the capsule shell dissolves. The gel slowly releases the hormone over a few hours and this minimizes high peaks that may occur when a lactose filler is used and the drug is rapidly released.

Transdermal delivery of hormonal steroids offers a number of advantages over other modes of administration; it normally allows the use of small amounts of the hormone for a long-lasting effect by avoiding chemical or metabolic degradation of drugs that may occur in the gastrointestinal tract. Moreover, by bypassing the liver, transdermal delivery eliminates the potential drawbacks associated with hepatic steroid metabolism.
Estradiol is a naturally occurring steroidal estrogen that occurs as white or creamy white, small crystals or as a crystalline powder. It is odorless, hygroscopic and is practically insoluble in water but has a solubility of about 35.7 mg/mL in alcohol at 25°C. It should be stored in tight, light-resistant containers. In the body, estradiol is reversibly oxidized to estrone and both estradiol and estrone can be converted to estriol. Generally, estradiol is not used orally due to extensive first-pass hepatic metabolism. Estradiol is indicated in the treatment of atrophic vaginitis, atrophic dystrophy of vulva, menopausal symptoms, female hypogonadism, ovariectomy, primary ovarian failure, inoperable breast cancer, inoperable prostatic carcinoma, poorly differentiated carcinoma of breast, female hypogonadism, ovariectomy, primary ovarian failure, vaginal atrophy, and abnormal uterine bleeding due to hormone imbalance.

Estrone is a naturally occurring steroidal estrogen prepared either from the urine of pregnant mares or from the Mexican yam (Dioscorea). It occurs as small, white crystals or as a white to creamy white, crystalline powder that is odorless and is practically insoluble in water. It is soluble to the extent of 4 mg/mL in alcohol and is soluble in vegetable oils. In the body, estradiol is reversibly oxidized to estrone and both estradiol and estrone can be converted to estriol.

Estriol is a naturally occurring estrogen and is claimed to have a selective action on the cervix, vagina and vulva and to have relatively little effect on the endometrium. It is often given in combination with estrone and estradiol in estrogen replacement therapy. It is a crystalline powder that is practically insoluble in water but is soluble in alcohol and vegetable oils. In the body, estradiol is reversibly oxidized to estrone and both estradiol and estrone can be converted to estriol.

Progesterone is a naturally occurring progestin that occurs as a white or creamy white, crystalline powder that is practically insoluble in water, soluble in alcohol, sparingly soluble in vegetable oils, and exists as a polymorph that melts at 121°C. Progesterone is extensively metabolized by the liver and is not usually given by the oral route, with some exceptions. Store in tight, light-resistant containers.

Testosterone occurs as white or slightly creamy white crystals or crystalline powder that is odorless and stable in air. It is practically insoluble in water, soluble 1 g in 5 mL of ethanol, 2 mL of chloroform and 100 mL of ether. It is soluble in vegetable oils. It melts between 153 and 157°C. Testosterone is subject to photodegradation in the presence of light. Testosterone is not very bioavailable when given as an oral-swallow preparation, but it is absorbed when administered buccally and sublingually. The different esters of testosterone are hydrolyzed to free testosterone and, subsequently, are metabolized in the same way as testosterone itself. Testosterone is indicated as androgen replacement for delayed male puberty, postpartum breast pain and engorgement, inoperable breast cancer and male hypogonadism.

**SIDE EFFECTS OF THERAPY**

Side effects of HRT are listed in Table 4 and can often be minimized by alteration of the dose. It is important to determine if the side effects are estrogen or progesterone related and an appropriate adjustment made. With each dosage adjustment, sufficient time should be allowed for patient response before another adjustment.

**PATIENT COUNSELING**

Inherent in the success of treating menopausal patients is taking the time for thorough education, which starts with patient assessment. One must know the patient’s history and the family history (presence of breast cancer, cardiovascular disease or osteoporosis). Individual files should be maintained on each patient.

Dietary recommendations are important and should include reduced fat and plenty of fresh vegetables, legumes and whole grains. Another important component is exercise, which helps in building stronger bones, increases the immune system function, decreases depression and anxiety and can actually reduce many symptoms of premenstrual syndrome and menopause.

**MARKETING HRT**

Education programs can be provided to doctors and nurses as well as to the lay public. Promotional materials concerning educational programs can be provided to places where women gather. Formal or informal seminars have been very successful in presenting the topic. Pharmacists providing these seminars generally begin with a short story of their pharmacy, the importance and legal aspects of compounding, the purposes of estrogens, progestins and androgens, compliance issues and compensation and insurance billing. These are often followed up by one-on-one personal consultations. After a personal consultation, many pharmacists follow up with a communication to the physician and/or nurse by telephone or fax.

**PATIENT FILES**

A consultation is an excellent way to start the process of patient history review and the use of a symptoms chart. In addition, laboratory test values can be maintained in this chart. While laboratory tests such as serum levels, saliva levels and urine monitoring have their place in patient evaluation, they do have limitations. However, using laboratory analysis in combination with clinical observation pharmacists can better recommend starting doses and dosage adjustments of hormone replacement for patients. The symptoms chart characterizes symptoms of estrogen excess, estrogen deficiency, progesterone excess and progesterone deficiency. This chart can be used during an initial patient consultation to determine a woman’s supplemental hormonal needs and then again on subsequent visits to determine if the woman’s prescribed dosages are meeting or exceeding her hormone requirements. The symptoms list chart is a tool which can be used to evaluate patients for their starting hormone dosages and a tool that can be used to evaluate the effectiveness of current hormone regimes. Pharmacists wishing to help women with their hormone needs should use all available tools including but not limited to family history evaluation, symptoms list chart, serum or saliva levels, bone density monitoring and uterine lining monitoring to completely assess the needs of their patients.

**MOST COMMONLY COMPOUNDED HRT PREPARATIONS**

There are numerous HRT formulations being compounded today. Among the most common are Progesterone Capsules, Progesterone Topical Creams, Testosterone Topical Creams, Triple Estrogen Capsules, Triple Estrogen with Progesterone Capsules, Progesterone Slow Release Capsules, Progesterone Vaginal Suppositories, Triple Estrogen with Progesterone and Testosterone Capsules, Progesterone in a Pluronic-Lecithin Organogel, Double Estrogen Capsules, Progesterone Troches, and Testosterone Capsules.
FORMULATIONS

Rx Double Estrogen 2.5 mg Capsules (Estriol 2 mg, Estradiol 0.5 mg)

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estriol</td>
<td>200 mg</td>
</tr>
<tr>
<td>Estradiol</td>
<td>50 mg</td>
</tr>
<tr>
<td>Lactose OR</td>
<td>39.75 g</td>
</tr>
<tr>
<td>Starch OR</td>
<td>37.25 g</td>
</tr>
<tr>
<td>Methocel E4M with</td>
<td>10 g</td>
</tr>
<tr>
<td>Lactose</td>
<td>23.75 g</td>
</tr>
</tbody>
</table>

Procedure for the above capsules (Each formula is for 100 #1 capsules)
1. Blend the estriol and estradiol powders together.
2. Geometrically, incorporate the lactose or starch and mix thoroughly, OR
3. Geometrically, incorporate the Methocel E4M, then the lactose and mix thoroughly.
4. Encapsulate 100 capsules, using a size #1 capsule.
5. Check the weights of at least 10 capsules.
6. Package and label.

Rx Triple Estrogen 2.5 mg Capsules (Estriol 2 mg, Estrone 0.25 mg, Estradiol 0.25 mg)

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estriol</td>
<td>200 mg</td>
</tr>
<tr>
<td>Estrone</td>
<td>25 mg</td>
</tr>
<tr>
<td>Estradiol</td>
<td>25 mg</td>
</tr>
<tr>
<td>Lactose OR</td>
<td>39.75 g</td>
</tr>
<tr>
<td>Starch OR</td>
<td>37.25 g</td>
</tr>
<tr>
<td>Methocel E4M with</td>
<td>10 g</td>
</tr>
<tr>
<td>Lactose</td>
<td>23.75 g</td>
</tr>
</tbody>
</table>

Procedure for the above capsules (Each formula is for 100 #1 capsules)
1. Blend the estrone and estradiol powders together.
2. Incorporate the testosterone powder.
3. Geometrically, incorporate the lactose or starch and mix thoroughly OR
4. Geometrically, incorporate the Methocel E4M, then the lactose and mix thoroughly.
5. Encapsulate 100 capsules, using a size #1 capsule.
6. Check the weights of at least 10 capsules.
7. Package and label.

Rx Triple Estrogen 2.5 mg, Progesterone 100 mg and Testosterone 1 mg Capsules

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estriol</td>
<td>200 mg</td>
</tr>
<tr>
<td>Estradiol</td>
<td>25 mg</td>
</tr>
<tr>
<td>Estrone</td>
<td>25 mg</td>
</tr>
<tr>
<td>Progesterone</td>
<td>10 g</td>
</tr>
<tr>
<td>Testosterone</td>
<td>100 mg</td>
</tr>
<tr>
<td>Lactose</td>
<td>32.5 g   (#1 capsule)</td>
</tr>
</tbody>
</table>

Procedure for the above capsules (Each formula is for 100 #1 capsules)
1. Mix the estradiol and estrone powders thoroughly.
2. Incorporate the testosterone powder.
3. Incorporate the estradiol powder.
4. Incorporate the progesterone powder and mix.
5. Incorporate the lactose and thoroughly mix.
6. Encapsulate 100 capsules using a size #1 capsule.
7. Check the weights of at least 10 capsules.
8. Package and label.

Rx Progesterone 5% Cream

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progesterone, micr.</td>
<td>5 g</td>
</tr>
<tr>
<td>Glycerin</td>
<td>qs</td>
</tr>
<tr>
<td>Dermabase</td>
<td>95 g</td>
</tr>
</tbody>
</table>

Procedure:
1. Levigate the micronized progesterone with a small quantity of glycerin to form a smooth paste.
2. Geometrically, incorporate the Dermabase and mix until uniform and smooth.
3. Package and label.

Rx Progesterone 200 mg/mL in Pluronic Lecithin Organogel

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progesterone, Micronized</td>
<td>20 g</td>
</tr>
<tr>
<td>Propylene Glycol</td>
<td>20 mL</td>
</tr>
<tr>
<td>Lecithin:Isopropyl Palmitate Solution*</td>
<td>20 g</td>
</tr>
<tr>
<td>Pluronic F127 20% Gel**</td>
<td>qs 100 mL</td>
</tr>
</tbody>
</table>

Procedure:
1. Prepare a paste of the micronized progesterone and the propylene glycol.
2. Add the Lecithin:Isopropyl Palmitate Solution and mix well.
3. Add sufficient pluronic F127 20% gel to volume and mix well.
4. Package and label.

*The Lecithin: Isopropyl Palmitate Solution can be prepared by mixing 10 g of soy lecithin and 10 g of Isopropyl palmitate; allow to stand overnight for complete dissolution to occur.

**The Pluronic F127 20% Solution can be prepared by adding 20 g of pluronic F127 to sufficient cold (ice) water to make 100 mL. For complete dissolution, place in a refrigerator and allow to stand with periodic agitation.
Table 1. The phases of the menstrual cycle.

<table>
<thead>
<tr>
<th>Days</th>
<th>Phase</th>
<th>Hormonal Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4</td>
<td>Menstruation</td>
<td>Rising estrogen levels</td>
</tr>
<tr>
<td>5-8</td>
<td>Postmenstruum</td>
<td>Peaking estrogen levels</td>
</tr>
<tr>
<td>9-12</td>
<td>Late postmenstruum</td>
<td>Falling estrogen levels</td>
</tr>
<tr>
<td>13-16</td>
<td>Ovulation</td>
<td>Low estrogen levels</td>
</tr>
<tr>
<td>17-20</td>
<td>Post ovulation</td>
<td>Rising estrogen and progesterone levels</td>
</tr>
<tr>
<td>21-24</td>
<td>Early premenstruum</td>
<td>Peak estrogen and progesterone levels</td>
</tr>
<tr>
<td>25-28</td>
<td>Premenstruum</td>
<td>Falling levels of estrogen and progesterone</td>
</tr>
</tbody>
</table>

Table 2. Symptoms associated with a decrease in estrogen.

- Anxiety
- Dry skin
- Heart palpitations
- Inability to reach orgasm
- Memory loss
- Night sweats
- Shortness of breath
- Vaginal dryness
- Yeast infections
- Depression
- Headache
- Hot flashes
- Lack of menstruation
- Mood swings
- Painful intercourse
- Sleep disorders
- Vaginal shrinkage

Table 3. Symptoms associated with a decrease in progesterone.

- Acne
- Anxiety
- Cramps
- Early menstruation
- Food cravings
- Headache
- Insomnia
- Low libido
- Painful breasts
- Swollen breasts
- Asthma
- Bloating
- Depression
- Emotional swings
- Fuzzy thinking
- Inability to concentrate
- Irritability
- Moodiness
- Painful joints
- Weight gain

Table 4. Side effects associated with HRT.

- Bloating
- Craving for sweets
- Fatigue
- Heavy/irregular menses
- Loss of sex drive
- Pounding headache, bilateral
- Recurrent vaginal yeast infections
- Vomiting
- Weight gain
- Breast enlargement and tenderness
- Depression
- Fibrocystic breasts
- Leg cramps
- Nausea
- Premenstrual-like mood swings
- Thinning of the hair
- Water retention
- Yellow-tinged skin

REFERENCES


Paddock is your source for compounding actives, compounding vehicles and professional support.

Vehicles:
Aquabase, Dermabase, Fattibase, Hydrocream, LiquaDerm-A, Liqua-Gel, Ora-Plus, Ora-Sweet, Ora-Sweet SF, Polybase, Suspendol-S

Actives:
Colistin, Dexamethasone, Erythromycin, Hydrocortisone, Hydromorphone, Morphine, Neomycin, Polymixin B, Progesterone, Testosterone, Triamcinolone... & others
INTRODUCTION

Many pharmacists and pharmacy technicians have a tendency to pay more attention to active drug substances in formulations and to minimize the importance of the excipients. However, excipients can dramatically alter the physical and chemical stability as well as the therapeutic effectiveness of the final drug preparation. Excipients can affect bioavailability, rate of drug release for all dosage forms, duration of action for many dosage forms, extent of penetration for many topicals/transdermals, and one of the most important considerations, patient compliance.

Two commonly used excipients in various dosage forms include glycine and propylene glycol. These two substances are chemically related as they both contain three carbons; the primary difference is that one contains two hydroxyl groups and the other contains three (See Figure 1). The series of substances that are official in the USP could be viewed as starting with isopropanol with one hydroxyl group on the middle carbon atom, progressing to propylene glycol, with two hydroxyl groups, and then to glycerin with three hydroxyl groups. Glycerin and propylene glycol have been used in pharmacy for over one hundred years and are extensively used in pharmaceutical compounding today.

GLYCERIN

Properties

Glycerin is the simplest trihydric alcohol. It was discovered by Scheele in 1779, who called it the “sweet principle of fats.” Glycerin is the alcohol present in the esters (glycerides) of oils and fats from which it may be released by saponification. It was more fully investigated by Chevreul who named it “glycerine” and it came into use in medicine and pharmacy about 1846. It was first obtained in the United States on a commercial scale, from the washings of lead plaster, by Shoemaker of Philadelphia.

Glycerin (C₃H₈O₃) occurs as a clear, colorless, syrupy liquid with a sweet warm taste, approximately 0.6 times as sweet as sucrose. It has not more than a slight characteristic odor, which is neither harsh nor disagreeable. It is hygroscopic and its solutions are neutral to litmus. It is miscible with water and with alcohol but is insoluble in chloroform, ether and in fixed and volatile oils. It has a solubility at 20°C as follows: acetone (slightly soluble); benzene (practically insoluble); ethyl acetate (1 in 11); methanol (soluble). It boils at 290°C with decomposition and melts at 17.8°C. It has a specific gravity of not less than 1.249. A 2.6% v/v aqueous solution is iso-osmotic with serum. It should be preserved in tight containers.

Glycerin USP contains not less than 99.0% and not more than 101.0% of C₃H₈O₃, calculated on the anhydrous basis. Official USP products include Glycerin Ophthalmic Solution USP, Glycerin Oral Solution USP and Glycerin Suppositories USP.

Uses

Glycerin is categorized in the NF as a humectant, plasticizer, solvent and tonicity-adjusting agent. It is listed as being used as an antimicrobial preservative emollient, humectant, plasticizer, solvent, sweetening agent and tonicity-adjusting agent. Topically, it is used as a humectant and emollient. Parenterally, it is used primarily as a solvent. In oral preparations, it is used as a solvent, sweetening agent, antimicrobial preservative and viscosity-increasing agent. In film coatings and in the preparation of soft gelatin capsules and gelatin suppositories, it is used as a plasticizer. It is also used in a number of therapeutic applications.
Glycerin is also used in the manufacturing of dynamite, cosmetics, soaps, confectioneries, blacking, printing and copying inks, lubricants, elastic glues, lead oxide cements, antifreeze, gas meters, hydraulic jacks, shock absorber fluid, ice collars, ice bags and as a fermentation nutrient in the production of antibiotics.7

Glycerin is an excellent solvent, but its range is not as extensive as that of water or alcohol. It is a solvent for fixed alkalies, a large number of salts, vegetable acids, pepsin, tannin, some active principles of plants, gums, soluble carbohydrates and starch.

Orally, glycerin is readily absorbed from the intestine and is metabolized to carbon dioxide and glycogen or is used in the synthesis of body fats. Therapeutically, glycerin is used in large doses (70-80 g over 30-60 minutes) to reduce cranial pressure. Slow administration has no effect on the corneal edema but this effect is only transient, primarily for the management of acute glaucoma. Glycerin is also applied topically to reduce intraocular pressure and vitreous hemoglobinuria and renal failure. Glycerin is used orally in doses of 1.0 to 1.5 g/kg body weight to reduce intraocular pressure and vitreous volume before and after ophthalmic surgery, and as an adjunct in the management of acute glaucoma. Glycerin is also applied topically to reduce corneal edema but this effect is only transient, primarily for facilitating ocular examination and diagnosis. Oral doses are demulcent and can be mildly laxative, promoting fecal evacuation in the management of constipation; usually acting within 15 to 30 minutes. It is classified as an osmotic laxative but may also act through local irritant effects. Glycerin has lubricating and softening effects as well. Glycerin is used in ear drops for the removal of ear wax for its lubricating and softening action.

Adverse Effects

Often the adverse effects of glycerin are due to its dehydrating properties. In contact with mucous membranes, glycerin absorbs moisture and causes temporary irritation; this is the action primarily responsible for the effectiveness of glycerin when applied rectally in suppository form to produce fecal discharge in habitual constipation. Glycerin suppositories contain 91% glycerin and 9% sodium stearate. Headache, thirst, nausea, vomiting and hyperglycemia can be caused by oral administration of large doses.8

Safety

Glycerin is Generally Recognized as Safe (GRAS) and is listed in the FDA Inactive Ingredients Guide for use in inhalations; injections; nasal and ophthalmic preparations; oral capsules, solutions, suspensions and tablets; otic, rectal, topical, transdermal, and vaginal preparations.9

Dosage Forms

Glycerin is used in almost every dosage form available today. From a plasticizer in film coatings of tablets, to a solvent, preservative and sweetener in oral liquid dosage forms and in injections. An older dosage form, the glycerogelatins, were actually the forerunner of some contemporary dosage forms containing glycerin.

Glycerogelatins are plastic masses, composed of gelatin, glycerin and water, and a medicament suitable for application to the skin. For application, they are softened using heat and then painted on the surface with a brush. The combination of glycerin, gelatin and water has been further refined and the combination is now used as the basis of glycerin suppositories and soft, chewable gummy bears or chewable troches. Glycerinated gelatin suppositories have been used as vaginal suppositories and soft, chewable gummy bears or chewable troches. Glycerogelatins are plastic masses, composed of gelatin, glycerin and water, and a medicament suitable for application to the skin. For application, they are softened using heat and then painted on the surface with a brush. The combination of glycerin, gelatin and water has been further refined and the combination is now used as the basis of glycerin suppositories and soft, chewable gummy bears or chewable troches. Glycerinated gelatin suppositories have been used as vaginal suppositories and soft, chewable gummy bears or chewable troches. Glycerogelatins are plastic masses, composed of gelatin, glycerin and water, and a medicament suitable for application to the skin. For application, they are softened using heat and then painted on the surface with a brush. The combination of glycerin, gelatin and water has been further refined and the combination is now used as the basis of glycerin suppositories and soft, chewable gummy bears or chewable troches. Glycerinated gelatin suppositories have been used as vaginal suppositories and soft, chewable gummy bears or chewable troches.

Stability

Pure glycerin, under ordinary storage conditions, is not prone to oxidation by the atmosphere. However, it does decompose on heating evolving toxic acrolein. Mixtures of glycerin with water, ethanol and/or propylene glycol are chemically stable. It should be stored in an airtight container in a cool, dry place. If stored at low temperatures, it may crystallize; but it will become a solution when warmed to 20º C. When mixed with strong oxidizing agents, glycerin may explode. Examples of strong oxidizing agents include chromium trioxide, potassium chloride and potassium permanganate. In contact with zinc oxide or basic bismuth nitrate, black discoloration of glycerin occurs. Sometimes glycerin may contain an iron contaminant that can cause a darkening in color of mixtures containing phenols, salicylates and tannin. With boric acid, glycerin forms a boric acid complex called glyceroboric acid that is a stronger acid than boric acid.15

**PROPYLENE GLYCOL**

Properties

Propylene glycol came into use as a suggested replacement for glycerin when glycerin was in short supply during World War II. Its solvent and preservative properties at least in some instances combine the advantages of both glycerin and ethyl alcohol. It is often a better solvent than glycerin and also has greater power to inhibit mold growth and fermentation, being equal to ethyl alcohol for the latter purposes. An example of where propylene glycol has replaced glycerin is shown in a prior formulation for Hydrophilic Ointment, USP. Glycerin imparted a “softening” effect to the ointment when it was triturated; the use of propylene glycol corrected this problem.4,6

Propylene Glycol USP (C3H8O3, 1,2-Propanediol; 1,2-Dihydroxypropane, 2,2-Dihydroxypropanol; methyl ethylene glycol; methyl glycol; propane-1,2-diol, MW 76.09) contains not less than 99.5% of C3H8O3. It should be preserved in tight, light-resistant containers in a cool, dry place. It has a specific gravity between 1.035 and 1.037. It has a boiling point of 188º C and a melting point of 59º C. It occurs as a clear, colorless, viscous, practically odorless liquid with a slight, characteristic taste resembling that of glycerin. It absorbs moisture when exposed to moist air. It is miscible with water, acetone and with chloroform. It is soluble in ether (1 in 6 parts) and will dissolve many essential oils but is immiscible with fixed oils and light mineral oil. It is miscible with acetone, chloroform, ethanol (95%), glycerin and water. A 2.0% v/v aqueous solution is iso-osmotic with serum.4,6,8

Uses

Propylene glycol is classified in the NF as a humectant, plasticizer and solvent. Its functional category is as an antimicrobial preservative, disinfectant, humectant, plasticizer, solvent, stabilizer for vitamins and as a water-miscible cosolvent.4

Propylene glycol has been used as an aerosol antiseptic; when dispersed in air in concentrations as low as 1 part in 2,000,000 propylene glycol kills airborne staphylococci.7 In film-coating formulations, propylene glycol is used as a plasticizer. As a carrier, it is used with emulsifiers and as a vehicle for flavors, rather than using ethanol, since it is nonvolatile. Propylene glycol is also used in veterinary medicine as an oral glucogenic in ruminants.8 Other uses include as a nontoxic antifreeze in dairy establishments, substitute for ethylene glycol and glycerin, in the manufacture of synthetic resins and de-icing solutions, emulsifier in foods, solvent for food colors and flavors, humectic, solvent, as a mist to disinfect air and to create artificial smoke and mist for theatrical use.7 Overall, propylene glycol is a better solvent than glycerin and will dissolve a variety of drugs, including corticosteroids, phenols, sulfonamides, barbiturates, vitamins (A and D), most alkaloids and many local anesthetics. It is similar to ethanol as an antiseptic and is similar to glycerin in its activity against molds. It is only slightly less effective than ethanol.

Adverse Effects

Propylene glycol is generally regarded as a relatively nontoxic material and is extensively used in foods, drugs and cosmetics. Orally ingested propylene glycol is rapidly absorbed and is metabolized in the liver, primarily to lactic and pyruvic acids, and is also excreted unchanged in the urine.5,9 Topically, propylene glycol is more irritating than glycerin, but is regarded as minimally irritating. When applied to mucous membranes, it may produce some local irritation as well as when it is used under occlusive conditions. Otic preparations using propylene glycol have been reported to cause some local sensitivity.6 Injections containing high concentrations of propylene glycol may produce pain or irritation. Propylene glycol is approximately one-third as intoxicating as ethanol; administration of large volumes has been associated with adverse effects on the central nervous system as well as otoxicity, cardiovascular effects, seizures, hyperosmolarity and lactic acidosis. The World Health Organization has set an acceptable daily intake at up to 25 mg/kg of body weight. For intravenous administration, formulations containing 35% propylene glycol can cause hemolysis in humans.5
Safety
Propylene glycol has not been demonstrated to be teratogenic or mutagenic in humans. It is GRAS listed and is included in the FDA Inactive Ingredients Guide (oral, percutaneous preparations, IM and IV injections, inhalations; ophthalmic, rectal, topical and vaginal preparations).\(^8\)

Stability
Propylene glycol is stable when stored in a well-closed container but at high temperatures and exposed to air, it will oxidize yielding products such as propionaldehyde, lactic acid, pyruvic acid and acetic acid.\(^7\)

It should be stored in a well-closed container, protected from light, in a cool, dry place. Propylene glycol is chemically stable with ethanol (95%), glycerin and water. Its aqueous solutions may be autoclaved.

### Compounded Formulas Using Glycerin

**Vehicle-Plasticizer**

<table>
<thead>
<tr>
<th>Rx Chewable Lozenges/Troches/Gummy Bears</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gelatin Base (100 g)</strong></td>
</tr>
<tr>
<td>Gelatin</td>
</tr>
<tr>
<td>Glycerin</td>
</tr>
<tr>
<td>Methylparaben</td>
</tr>
<tr>
<td>Purified water</td>
</tr>
<tr>
<td><strong>Product (100 g)</strong></td>
</tr>
<tr>
<td>Gelatin base</td>
</tr>
<tr>
<td>Bentonite</td>
</tr>
<tr>
<td>Aspartame</td>
</tr>
<tr>
<td>Acacia powder</td>
</tr>
<tr>
<td>Citric acid monohydrate</td>
</tr>
<tr>
<td>Flavor</td>
</tr>
<tr>
<td>Active ingredient</td>
</tr>
</tbody>
</table>

**Gelatin Base:**
Using a water bath heated to boiling, insert a beaker or other suitable container and add the water, glycerin and methylparaben. Stir and heat for 5 minutes. Very slowly, over about 3 minutes, add the gelatin with stirring until it is thoroughly dispersed and free of lumps. Continue to heat for 45 minutes; remove from the heat, cool and refrigerate until used.

**Product:**
Calibrate the mold to be used for the prescription. Using a water bath, melt the gelatin base. Triturate all the powders together and add to the melted base and mix until evenly dispersed. Add the desired flavor, mix and pour into appropriate molds and allow to cool. Package and label.

**Dispensing/Wetting/Levigating Agent**

<table>
<thead>
<tr>
<th>Rx Rifabutin 20 mg/mL Oral Liquid (100 mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifabutin</td>
</tr>
<tr>
<td>Glycerin</td>
</tr>
<tr>
<td>Ora Plus</td>
</tr>
<tr>
<td>Ora Sweet</td>
</tr>
</tbody>
</table>

Empty 14 Mycobutin 150 mg capsules into a glass mortar. Pulverize the powder until uniform. Add the glycerin and mix until uniform. Add the Ora Plus in small portions and mix well. Add sufficient Ora Sweet to volume and mix well. Package and label.

<table>
<thead>
<tr>
<th>Rx Midazolam 2 mg/mL Oral Solution (100 mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam</td>
</tr>
<tr>
<td>Stevia</td>
</tr>
<tr>
<td>Sorbitol 70% solution</td>
</tr>
<tr>
<td>Glycerin</td>
</tr>
<tr>
<td>Flavor</td>
</tr>
<tr>
<td>Sodium benzoate</td>
</tr>
<tr>
<td>Purified water</td>
</tr>
</tbody>
</table>

Disperse the midazolam powder in about 70 mL of purified water. If necessary, add hydrochloric acid 2 N solution drop by drop to achieve a pH of 3.0, which is necessary to convert the midazolam to midazolam hydrochloride and continue to mix for 15 to 20 minutes. Add the stevia powder and sodium benzoate and mix well. Add the flavor to the glycerin and then to the mixture. Add the sorbitol and sufficient purified water to volume and mix well. Package and label.

<table>
<thead>
<tr>
<th>Rx Radiation Burn Mouth Rinse (100 mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Misoprostol</td>
</tr>
<tr>
<td>Glycerin</td>
</tr>
<tr>
<td>Diphenhydramine hydrochloride oral liquid</td>
</tr>
<tr>
<td>Lidocaine hydrochloride</td>
</tr>
<tr>
<td>Methylcellulose</td>
</tr>
<tr>
<td>Flavor</td>
</tr>
<tr>
<td>Preserved water</td>
</tr>
</tbody>
</table>

Pulverize the misoprostol tablets to a fine powder. Incorporate the lidocaine hydrochloride and methylcellulose powders together and add the glycerin to form a smooth paste. Add about 45 mL of preserved water and mix well. Add the diphenhydramine hydrochloride oral liquid, flavors and sufficient preserved water to volume and mix well. Package and label.

**Vehicle-Topical**

<table>
<thead>
<tr>
<th>Rx Glycerogelatin/Glycerinated Gelatin (100 g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gelatin</td>
</tr>
<tr>
<td>Glycerin</td>
</tr>
<tr>
<td>Purified water</td>
</tr>
</tbody>
</table>

Pour upon the gelatin sufficient distilled water to cover it, allow it to stand for one hour, pour off the water and allow the gelatin to drain for a few minutes. Transfer to a dish, add the glycerin and heat on a water bath until the gelatin is dissolved. Strain the solution while hot, transfer to a tared dish and heat on a water bath until the product weighs 100 g. When cooled, cut into pieces.

<table>
<thead>
<tr>
<th>Rx Glycerogelatin with Active Ingredient (100 g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycerinated gelatin</td>
</tr>
<tr>
<td>Glycerin</td>
</tr>
<tr>
<td>Distilled water</td>
</tr>
<tr>
<td>Active ingredient</td>
</tr>
</tbody>
</table>

Mix the active ingredient with the gelatin, add the water and incorporate this mixture with the glycerinated gelatin, which has been previously melted on a water bath. Continue to heat and stir until a homogeneous mixture is obtained. Pour into chilled molds and allow to congeal. Package and label.

**Vehicle-Rectal**

<table>
<thead>
<tr>
<th>Rx Glycerinated Gelatin Suppositories (100 g; number depends upon the mold used)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active drug</td>
</tr>
<tr>
<td>Purified water</td>
</tr>
<tr>
<td>Gelatin</td>
</tr>
<tr>
<td>Glycerin</td>
</tr>
</tbody>
</table>

Mix the active drug with the water; add the glycerin and mix well. Add the gelatin and heat on a water bath and mix well without incorporating air into the mixture. When the gelatin has dissolved, pour the melted mixture into chilled molds and allow to solidify. Package and label.

**Active Ingredient, Vehicle-Rectal**

<table>
<thead>
<tr>
<th>Rx Glycerin Suppositories (105 g; number depends upon the mold used)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycerin</td>
</tr>
<tr>
<td>Sodium stearate</td>
</tr>
<tr>
<td>Purified water</td>
</tr>
</tbody>
</table>

Heat the glycerin in a suitable container to about 120° C. Dissolve the sodium stearate in the heated glycerin. Add the purified water, mix and immediately pour into suitable molds. Cool until solidified and remove, if appropriate. Package and label.

Continued....
Vehicles:
Aquabase, Dermabase, Fattibase, Hydrocream, LiquaDerm-A, Liqua-Gel, Ora-Plus, Ora-Sweet, Ora-Sweet SF, Polybase, Suspendol-S

Actives:
Colistin, Dexamethasone, Erythromycin, Hydrocortisone, Hydromorphone, Morphine, Neomycin, Polymixin B, Progesterone, Testosterone, Triamcinolone... & others
**COMPounded Formulas USING PROPYLENE Glycerol**

**Dispersing/Wetting/Solubilizing Agent**

**Rx Acyclovir and Chlorhexidine Cold Sore Gel (10 g)**

- Acyclovir 1 g
- Chlorhexidine digluconate 200 mg
- Hydroxypropyl methylcellulose 300 mg
- Propylene glycol 1 mL
- Preserved water 8 mL

Accurately weight or measure each of the ingredients. Mix the acyclovir and hydroxypropyl methylcellulose with the propylene glycol. Slowly incorporate the preserved water and the chlorhexidine digluconate solution (1 mL of a 20% solution) and mix well.

**Vehicle/Solubilizer/Viscosity Enhancer**

**Rx 5-Aminosalicylic Acid Enema (100 mL)**

- 5-Aminosalicylic acid 4 g
- Sodium phosphate dibasic, anhydrous 400 mg
- Sodium phosphate monobasic anhydrous 4.5 g
- Sodium chloride 9 g
- Sodium ascorbate 500 mg
- Tragacanth 4 g
- Methylparaben 2 g
- Propylparaben 500 mg
- Propylene glycol 25 mL
- Distilled water qs 100 mL

Dissolve the parabens in the propylene glycol with stirring. Add the tragacanth to this solution and mix well. Package and label. Note: The propylene glycol is used as an aid in incorporating the 5-aminosalicylic acid and hydroxypropyl methylcellulose into the aqueous system.

**Vehicle-Solubilizer-Penetration Enhancer**

**Rx Hydrocortisone Gel**

- Hydrocortisone 1 g
- Carbomer 934 1.5 g
- Trolamine 250 mg to 350 mg
- Propylene glycol qs 100 g

Accurately weigh the hydrocortisone and carbomer 934. Mix the hydrocortisone with about 95 g of propylene glycol. Add the carbomer 934 and mix well. Slowly add the trolamine until the desired viscosity is obtained. Add additional propylene glycol to make 100 g and mix well. Package and label.

**Vehicle-Solubilizer-Penetration Enhancer**

**Rx Antipruritic Clear Lotion (100 mL)**

- Liquified phenol 0.4 mL
- Tannic acid 8.4 g
- Benzoin 2.2 g
- Ethanol 65 mL
- Propylene glycol 20 mL
- Purified water qs 100 mL

Add the liquefied phenol to a clean mortar. Add the ethanol and mix well. Add the tannic acid and mix until finely dispersed. Add the benzoin and propylene glycol. Add sufficient purified water to volume and thoroughly mix. Package and label.

**Vehicle-Penetration Enhancer-Viscosity Enhancer**

**Rx Psoriasis Lotion (100 mL)**

- Coal tar solution 5 mL
- Salicylic acid 5 g
- Urea 10 g
- Triamcinolone acetonide 160 mg
- Propylene glycol qs 100 mL

Dissolve the urea and salicylic acid in about 75 mL of propylene glycol; this may take 30 to 45 minutes. Add the triamcinolone acetonide and mix well. Incorporate the coal tar solution and mix well. Add sufficient propylene glycol to make 100 mL and thoroughly mix. Package and label.

**Vehicle-Solubilizer-Penetration Enhancer**

**Rx Progesterone 50 mg/mL Topical Solution (100 mL)**

- Progesterone 5 g
- Benzyl alcohol 20 mL
- Dimethylsulfoxide 20 mL
- Absolute alcohol 20 mL
- Propylene glycol qs 100 mL

Combine the benzyl alcohol, dimethylsulfoxide and absolute alcohol and mix well. Add the progesterone and sufficient propylene glycol to volume and mix well. Package and label.

**Vehicle-Penetration Enhancer**

**Rx Analgesic Stick (100 g)**

- Menthol 15 g
- Sodium salicylate 35 g
- Sodium stearate 13 g
- Benzyl alcohol 1.5 g
- Sterile water for injection qs 100 mL

Dissolve the diazepam in a mixture of the propylene glycol and ethyl alcohol. Add the sodium benzoate, benzoic acid and benzyl alcohol to about 30 mL of sterile water for injection. Combine the two liquids. Adjust the pH if necessary to the range of 6.2 to 6.9. Add sufficient sterile water for injection to volume and mix well. Filter through a sterile 0.2 µm filter into sterile vials. Package and label; test appropriately.
Water 12 g
Propylene glycol 25 g

Gently heat and melt the sodium stearate. Mix the water with the propylene glycol and add to the melted sodium stearate. Mix thoroughly, remove from heat, and allow this base to cool slightly. Dissolve the menthol in the methyl salicylate and add to the base slowly, with thorough mixing. As the product begins to thicken, continue mixing and pour into stick-type containers.

Table 1: Comparison of the Uses of Glycerin and Propylene Glycol

<table>
<thead>
<tr>
<th>Use</th>
<th>Dosage Form</th>
<th>Concentration (%) Glycerin</th>
<th>Propylene Glycol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emollient</td>
<td>Topicals</td>
<td>≤ 30</td>
<td>~15</td>
</tr>
<tr>
<td>Humectant</td>
<td>Topicals</td>
<td>≤ 30</td>
<td>15-30</td>
</tr>
<tr>
<td>Preservative</td>
<td>Solutions, Semisolids</td>
<td>≤ 20</td>
<td>15-30</td>
</tr>
<tr>
<td>Solvent/Cosolvent</td>
<td>Aerosol solutions</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oral solutions</td>
<td>--</td>
<td>10-25</td>
</tr>
<tr>
<td></td>
<td>Parenterals</td>
<td>≤ 50</td>
<td>10-60</td>
</tr>
<tr>
<td></td>
<td>Topicals</td>
<td>--</td>
<td>5-80</td>
</tr>
<tr>
<td>Ophthalmic Forms</td>
<td>0.5-3.0</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Plasticizer</td>
<td>Tablets</td>
<td>Variable</td>
<td>--</td>
</tr>
<tr>
<td>Sweetener</td>
<td>Elixirs</td>
<td>≤ 20</td>
<td>--</td>
</tr>
</tbody>
</table>

REFERENCES

INTRODUCTION
Psoriasis, a chronic scaling disease of the skin, affects between 1 and 2% of the population in the United States. It involves about 7 million individuals with between 150,000 and 260,000 new cases diagnosed each year.1 It primarily affects adults but does occur in all age groups; most common between the ages of 15 and 35. The economic impact of psoriasis can be significant, ranging from $1.6 billion to $3.2 billion spent annually on just treating psoriasis, not including the amount from the estimated 56 million hours of work lost each year.1 Psoriasis affects men and women about equally but may be slightly more prevalent in women. Patients with psoriasis may suffer discomfort (pain, itching), restricted motion in some of their joints or emotional distress. Psoriasis is generally a mild condition and there are many medications (prescription and nonprescription) that can be used to help alleviate the discomfort. Psoriasis is actually a non-contagious, chronic skin disease presenting in many different forms and many different levels of severity. When joints are involved, it is called psoriatic arthritis and is similar to rheumatoid arthritis. Individuals with psoriasis often experience a variety of emotions, including sadness, despair, guilt, anger and even low self-esteem. Sometimes they are embarrassed due to the unsightly patches of the disease and sometimes are frustrated at not knowing why they developed the disease or why it cannot be cured. In fact, psoriasis can even alter the employment of affected individuals.

DEFINITION OF PSORIASIS
Psoriasis is defined as "a common multifactorial inherited condition characterized by the eruption of circumscribed, discrete and confluent, reddish, silvery-scaled maculopapules; the lesions occur predominantly on the elbows, knees, scalp, and trunk, and microscopically show characteristic parakeratosis and elongation of rete ridges with shortening of epidermal keratinocyte transit time due to decreased cyclic guanosine monophosphate".2

CAUSE OF PSORIASIS
The actual cause of psoriasis is unknown but may be related to disorders in the body’s immune system; it is an immune-mediated disorder. Signals are generated which increase the growth rate and cycle in skin cells resulting in cells that accumulate on the surface of the body and they are not shed fast enough. Where normal skin cells mature in 28 to 30 days, a psoriatic cell may mature in

GOALS AND OBJECTIVES
Goal: To provide compounding pharmacists supportive information on the prevalence, diagnosis, symptoms and treatment of psoriasis.

Objectives: After reading and studying the article, the reader will be able to:
1. Define and discuss the different types of psoriasis.
2. Describe the different methods of treating psoriasis.
3. Discuss the active ingredients used in treating psoriasis.
4. Discuss the various formulations used in treating psoriasis.
generally involves isolated patches on the knees, elbows, and scalp. It involves less than about 2% of their body and is considered in the classification.

Mild psoriasis is experienced by about 75-80% of the population. It involves small patches that are usually dry and not thick. The psoriatic area is usually dry and exhibits symptoms of pain, itching, and cracking.

Guttate (Latin for "drop") psoriasis is indicated by the presence of small, red, individual "drops" on the skin, generally the trunk and limbs and sometimes the scalp. Guttate psoriasis lesions are generally not covered with scales and are generally not as thick as the plaque psoriasis.

Inverse (flexural) psoriasis is commonly found in the armpits, breasts, and folds of the skin around the genital area. It affects men and women equally and generally occurs between the ages of 30 and 50.

Plaque psoriasis (psoriasis vulgaris) is the most common, affecting about 80% of individuals suffering from the disorder. It appears on almost any skin surface, especially the elbows, scalp, knees, trunk, and nails. The lesions are described as well-defined patches of red, raised skin. The buildup on the patches, composed of dead skin cells, is called scale and appears flaky and silvery white. The scale constantly sheds as it becomes loose. The psoriatic area is usually dry and exhibits symptoms of pain, itching, and cracking.

Types of Psoriasis

Plaque psoriasis (psoriasis vulgaris) is the most common, affecting about 80% of individuals suffering from the disorder. It appears on almost any skin surface, especially the elbows, scalp, knees, trunk, and nails. The lesions are described as well-defined patches of red, raised skin. The buildup on the patches, composed of dead skin cells, is called scale and appears flaky and silvery white. The scale constantly sheds as it becomes loose. The psoriatic area is usually dry and exhibits symptoms of pain, itching, and cracking.

Guttate (Latin for "drop") psoriasis is indicated by the presence of small, red, individual "drops" on the skin, generally the trunk and limbs and sometimes the scalp. Guttate psoriasis lesions are generally not covered with scales and are generally not as thick as the plaque psoriasis.

Inverse (flexural) psoriasis is commonly found in the armpits, breasts, and skin folds around the genitals and buttocks. The appearance is smooth and dry but red and inflamed; it does not have the scales present. It is easily irritated from rubbing and sweating and is more common in overweight patients.

Erythrodermic psoriasis, the least common form of the disease, is particularly inflammatory and is characterized by periodic, widespread skin redness. This reddening and accompanying exfoliation, covering most of the body, is often accompanied by severe itching and pain.

Generalized pustular psoriasis (von Zumbusch Pustular Psoriasis), like it’s name, occurs widespread over the body but is a relatively rare form of the disease. The skin may become intensely painful and tender and pustules may appear, then dry up and reappear.

Localized pustular psoriasis is a more confined form of the disease. The pustules appear, turn brown and peel. One form is palmoplantar pustulosis that is characterized by large pustules in fleshy areas of the hands and feet. Psoriatic arthritis may develop in about 10 to 30% of patients with psoriasis. Symptoms can include stiffness, pain, swelling/tenderness of joints and soft tissue, reduced range of motion, morning stiffness and tiredness. Additional symptoms can include conjunctivitis and changes in the nails. Joints usually affected include the wrists, knees, ankles, lower back and neck. It affects men and women equally and generally occurs between the ages of 30 and 50.

Severity of Psoriasis

There are three categories of psoriasis that makes it easier to select treatment. The categories include (1) Mild Psoriasis, (2) Moderate Psoriasis and (3) Severe Psoriasis. Also, the way the psoriasis affects an individual’s quality of life is considered in the classification.

Mild psoriasis is experienced by about 75-80% of the patients. It involves less than about 2% of their body and generally involves isolated patches on the knees, elbows, and scalp. Hands and feet. Treatment often includes topical products, including moisturizers and OTC and Rx creams, ointments and shampoos, which are generally sufficient to control the symptoms.

Moderate psoriasis affects about 2-10% of the body's surface and involves the arms, legs, torso, scalp and other areas. Treatment includes topical medications, phototherapy and oral medications.

Severe psoriasis involves more than 10% of the body which may be covered with psoriasis plaques or pustules or widespread erythrodermic psoriasis; it can cause severe peeling of the skin. Patients with this category of psoriasis tend to develop psoriatic arthritis. Therapy includes phototherapy, oral medications or a combination.

The severity of psoriasis can be made worse by skin injury and irritation, sun exposure, stress and anxiety, some medications, infections and possibly diet.

Treatment of Psoriasis

Psoriasis is usually a lifelong, relapsing disease in which the main treatment goal is resolution of lesions. The treatment approaches are not curative but can be very effective in controlling the disease. The basic approaches to therapy involve a reduction in the rate of epidermal proliferation in addition to a decreased dermal inflammatory and immune response. An appropriate selection of therapy combined with compliance will usually result in a satisfactory outcome in a few days to a few weeks. The risk-benefit issues are very important when determining a treatment approach as is the recognition of the pathogenic factors involved. The main goal of treatment is to allow the patient to be functional in all aspects of their life and to maintain good physical and emotional health. Patients with limited disease can usually be managed with topical therapy. The selection of the treatment method is dependent upon a number of factors, including the type of psoriasis, its severity, patient's age and medical history and its location on the body. Generally a trial and error approach is utilized as individuals respond differently to therapy.

Topical therapy can include sunlight, moisturizers, baths, salicylic acid, retinoids, anthralin, coal tar preparations, calcipotriene, tacrolimus and corticosteroids. Sunlight in short, regular daily doses that do not produce a sunburn will clear up psoriasis in some cases. Moisturizers that are thick and greasy, or emollients, aid in hydrating the skin and reducing scaling and itching. They are generally used regularly and over a long time period.

Baths consisting of an oil (generally dispersed with the aid of a surfactant) added to the bath water can be soothing. Generally, the body is soaked for about 15 minutes in water containing a tar preparation, oiled oatmeal or Epsom salts. Salicylic acid, a keratolytic, aids in removing the scales. It is considered most effective when used in association with topical steroids, coal tar or anthralin. It is generally used in concentrations of 5-10% in ointment or cream vehicles. In cases of thick plaques, a stronger 20% concentration has been used.

Retinoids used topically, including tazarotene (Tazorac), can be effective. Tazorac is a fast-drying, clear gel that is topically applied. It has few side effects but does not act as quickly as the corticosteroids. Tazarotene, a vitamin A
derivative, is also very effective for psoriasis. It selectively binds to retinoic acid receptors which result in less local irritation and cytotoxicity than other topical retinoids.

Anthralin is an old remedy that is still possibly the most effective of all topical treatments. It works by reducing inflammation and keratinocyte proliferation. It is very effective in treating psoriasis but side effects such as erythema, burning and staining of the skin make it undesirable to patients. Short-contact application of newer anthralin creams can decrease these side effects. Its primary disadvantages are that it is messy and stains the clothing and skin. If it is applied to the skin for only short periods of time (eg 10 to 20 minutes) this minimizes the staining problems. It is often combined with a variety of topical drugs. Zinc oxide ointment or petrolatum can first be applied around the lesion followed by the anthralin preparation; this will minimize irritation to the normal skin surrounding the lesion. Anthralin preparations are generally applied in concentrations from 0.05% to 5% and is applied at night. Wearing plastic gloves and using old sheets and nightclothes will help to minimize its staining properties.

Coal tar preparations (the oldest treatment for psoriasis), described by the Greek philosopher Dioscorides nearly 2,000 years ago, are effective in treating psoriasis. Coal tar can contain up to 10,000 different chemical compounds and its precise mechanism of action is unknown. Coal tar has antiproliferative and anti-inflammatory actions and it has been demonstrated to be efficacious in the treatment of mild to moderate psoriasis. It can be used alone or in combination with other drugs and phototherapy (UVB). The use of coal tar preparations is limited by their main disadvantages; they are messy and smelly to use. Many of the newer purified tars in more elegant creams, ointments and gels are easier and more pleasant to use. Coal tar preparations seem to increase the effectiveness of UV light. They generally are applied at bedtime with sufficient time allowed for drying and then removed by showering in the morning. As an alternative, they can be applied in the morning, allowed to stay for 10-15 minutes, and then showered off.

Calcipotriene is a synthetic form of vitamin D3 and has been available since 1993. Calcipotriene ointment (Dovonex®) can control the excessive production of skin cells when used twice daily. It’s use may be based on the observation that hypocalcemia is present in many patients who develop various forms of psoriasis. It can irritate the skin and is not recommended for the face or groin area. About 60% of the patients have a good to excellent response after 4 months of treatment.

Corticosteroids are the choice of many physicians to begin therapy. The corticosteroid creams or ointments are easy to use and are a good choice for the scalp, face, ears and skin folds. However, these should not be used for too long a time period. The adverse effects and mechanism of actions vary greatly between the available topical agents. Chronic use of topical steroids can result in decreased effectiveness, local tissue atrophy and systemic glucocorticoid effects. Therefore, topical steroids should only be instituted as an adjunct to therapy if long-term use is required.

Phototherapy involves ultraviolet light; some of the artificial sources of UVB light are similar to natural sunlight. There are some newer phototherapy light sources available, called narrow-band UVB, that emit the part of the UV spectrum that is most beneficial for psoriasis. Generally, phototherapy is used after topical treatments, even though some physicians actually start with phototherapy. UVB light boxes can be used either at the physician’s office or at home.

Combination phototherapy can involve the use of psoralen and ultraviolet A light (PUVA). Psoralen serves to enhance the sensitivity of the body to this light and is used when more than 10% of the skin is affected or whenever a quick response is required as when the disease is interfering with an individual’s occupation. PUVA treatments two or three times weekly appear to be more reliable in clearing psoriasis than UVB treatments; however, they are associated with increased short-term side effects, including nausea, headache, fatigue, burning and itching.

If topical therapies fail or the disease is severe, systemic treatment can be instituted. Some common systemic therapies include methotrexate, acitretin, cyclosporin, hydroxyurea and antibiotics.

Methotrexate, which may work through immunomodulation, is effective for severe disease but is limited by its severe side effects and possible mutagenic effects. These patients must be closely monitored and methotrexate should not be used in patients with long-term liver disease or anemia.

Acitretin, a systemic retinoid is useful in erythrodermic, chronic, and pustular psoriasis. The main concerns with this medication are teratogenicity and hyperlipidemia. Careful patient selection and laboratory monitoring increase the safety of acitretin.

Cyclosporin is an immune suppressant that slows rapid cell growth. It provides rapid symptomatic relief but is effective only as long as the treatment lasts. Patients with severe psoriasis or those that are refractory to other systemic therapies are generally the best candidates for cyclosporin. Side effects such as hypertension and renal toxicity may limit its use.

Hydroxyurea is not as toxic as methotrexate and cyclosporine but it is also not as effective. It can be combined with PUVA or UVB. Side effects include anemia and a decrease in white blood cells and platelets.

Antibiotics are not routine treatment for psoriasis but can be prescribed whenever an infection triggers the outbreak of the disease.

### USEFUL FORMULATIONS FOR TREATING PSORIASIS

**Rx  Psoriasis Moisturizing Ointment**

- Cocoa butter 50 g
- White petrolatum 40 g
- White wax 10 g

1. Calculate the required quantity of each ingredient for the amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Melt the white petrolatum and white wax at the lowest possible temperature and mix well.
4. Add the cocoa butter and mix while cooling.
5. Package and label.

**Rx  Coal Tar 5% Ointment**

- Crude coal tar 5 g
- Polysorbate 80 30 g
- White petrolatum 65 g

1. Calculate the required quantity of each ingredient
for the amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Mix the crude coal tar with the polysorbate 80 until uniform.
4. Incorporate that mixture into the white petrolatum, geometrically, and mix until smooth and uniform.
5. Package and label.

Rx Coal Tar Gel
Coal tar solution 2 mL
Carbopol 940 500 mg
Ethanol 70% qs 100 mL
Trolamine qs to pH 6.5
1. Calculate the required quantity of each ingredient for the amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Disperse the Carbopol 940 in the ethanol and mix well.
4. Dropwise, add the trolamine until a pH of about 6.5 is obtained.
5. Incorporate the coal tar solution and mix well.
6. Allow to set until gelling is complete and mix until smooth, if necessary.
7. Package and label.

Rx Salicylic Acid and Coal Tar Cream
White Petrolatum 20 g
Laonil alcohol 1.5 g
Cetearyl alcohol 10 g
Stearoyl alcohol 3 g
Coal tar solution 5 g
Salicylic acid 5 g
Propylene glycol 10 mL
Methylparaben 200 mg
Propylparaben 100 mg
Purified water qs 100 mL
1. Calculate the required quantity of each ingredient for the amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Melt the petrolatum, lanolin alcohol, cetearyl alcohol and stearoyl alcohol at about 55 to 60°C.
4. Heat the purified water to about 55 to 60°C and add the methylparaben and propylparaben.
5. Add step 4 to step 3 and mix well. Cool to about 35°C.
6. Mix the coal tar solution and propylene glycol and add the salicylic acid and mix well.
7. Incorporate the mixture into the cooled cream base and mix well.
8. Package and label.

Rx Coal Tar Medication Stick
Coal Tar Solution 5 mL
Propylene glycol 13.5 g
Sodium stearate 1.5 g
1. Calculate the required quantity of each ingredient for the amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Heat the propylene glycol and sodium stearate at about 80-85°C until dissolved.
4. Allow the mixture to cool to about 60°C and add the coal tar solution with mixing.
5. Cool with intermittent stirring and pour into applicator tubes just prior to solidification.
6. Package and label.

Rx Coal Tar and Salicylic Acid in Almond Oil Lotion
Salicylic acid 2 g
Coal Tar Solution 3 mL
Ethoxy diglycol 8 mL
Almond oil qs 100 mL
1. Calculate the required quantity of each ingredient for the amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Wet the salicylic acid with the ethoxydiglycol.
4. Incorporate the coal tar solution and mix well.
5. Add sufficient almond oil slowly with mixing to volume and mix well.
6. Package and label.

Rx Coal Tar and Hydrocortisone Lotion
Coal tar solution 3 mL
Hydrocortisone 500 mg
Cetyl alcohol 2 g
Lanolin, Anhydrous 1 g
Mineral oil, Light 12 mL
Polysorbate 80 3 g
Propylene glycol 10 mL
Purified water qs 100 mL
1. Calculate the required quantity of each ingredient for the amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Comminute the salicylic acid to a fine powder.
4. Add the coal tar solution and Span 80 and mix well.
5. Incorporate sufficient heavy mineral oil to volume and mix well.
6. Package and label.

Rx Coal Tar Bath Solution
Coal tar solution 7 g
Polysorbate 80 35 mL
Span 80 15 mL
Lavender oil qs
Mineral oil, light qs 100 mL
1. Calculate the required quantity of each ingredient for the amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Mix the coal tar solution and hydrocortisone.
4. Add the propylene glycol and mix well.
5. Melt the cetyl alcohol, lanolin and mineral oil together.
6. Add the polysorbate 80 to the melted mixture.
7. Warm 150 mL of water to 60°C and add to the melted oil phase.
8. Add the coal tar:hydrocortisone mixture and mix well.
9. Cool and stir until congealed.
10. Package and label.
Rx  Tacrolimus 0.03% or 0.1% Ointment
Tacrolimus 30 mg 100 mg
Aquabase™ qs 100 g 100 g
1. Accurately weigh/measure each of the ingredients.
Capsules can be used as the source of the Tacrolimus.
2. Empty the capsules and pulverize the powder.
3. Using either propylene glycol or ethoxy diglycol, make a smooth paste.
4. Incorporate the hydrophilic petrolatum geometrically to volume and mix well.
5. Package and label.

REFERENCE

Rx  Coal Tar, Benzocaine and Salicylic Acid Lotion
Coal tar solution 48.5 mL
Salicylic acid 1 g
Benzocaine 2 g
Ethanol 95% qs 100 mL
1. Calculate the required quantity of each ingredient for the amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Dissolve the salicylic acid in 10 mL of ethanol.
4. Dissolve the benzocaine in 25 mL of ethanol.
5. Combine the two solutions and add the coal tar solution.
6. Add sufficient ethanol to volume and mix well.
7. Package and label.

Rx  Zinc Pyrithione and Clobetasol Shampoo
Zinc pyrithione 200 mg
Clobetasol 17 dipropionate 50 mg
Menthol 250 mg
Ethanol 95% 2 mL
Shampoo vehicle qs 100 mL
1. Calculate the required quantity of each ingredient for the amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Dissolve the menthol in the ethanol.
4. Add the zinc pyrithione and clobetasol 17 dipropionate and mix well.
5. Incorporate sufficient shampoo vehicle to volume and mix well.
6. Package and label.

Rx  Zinc Pyrithione 0.2% and Clobetasol 0.05% Lotion
Zinc pyrithione 1 g
Clobetasol propionate 10 mL
Isopropyl alcohol 91% 20 mL
Isopropyl myristate qs 80 mL
1. Calculate the required quantity of each ingredient for the amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Levigate the anthralin with the castor oil until a smooth mixture is obtained.
4. Geometrically, incorporate the white petrolatum and mix until smooth and uniform.
5. Package and label.

Rx  Anthralin 1% Ointment
Anthralin 1 g
Castor oil 10 mL
White petrolatum qs 100 g
1. Calculate the required quantity of each ingredient for the amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Levigate the anthralin with the castor oil until a smooth mixture is obtained.
4. Geometrically, incorporate the white petrolatum and mix until smooth and uniform.
5. Package and label.

Rx  Anthralin 0.1% and Salicylic Acid 0.5% Cream
Anthralin 100 mg
Salicylic acid 500 mg
Glycerin qs
Dermabase™ qs 100 g
1. Calculate the required quantity of each ingredient for the amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Mix the anthralin and salicylic acid and ensure the particle size is small and uniform.
4. Incorporate a small quantity of glycerin to form a smooth paste.
5. Geometrically, incorporate the Dermabase™ and mix well.
6. Package and label.

Rx  Anthralin 0.2% and Salicylic Acid 2% Scalp Lotion
Anthralin 200 mg
Salicylic acid 2 g
Peanut oil 50 mL
Coal tar solution 50 mL
1. Calculate the required quantity of each ingredient for the amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Dissolve the anthralin and the salicylic acid in the coal tar solution.
4. Incorporate the peanut oil and mix well.

Rx  Methoxsalen 0.3% Topical Solution
Methoxsalen 300 mg
Propylene glycol 45 mL
Ethanol 95% qs 100 mL
1. Calculate the required quantity of each ingredient for the amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Dissolve the methoxsalen in the propylene glycol.
4. Add sufficient ethanol 95% to volume and mix well.
5. Package and label.
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