



Translabial route: As a platform for systemic drug delivery

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ABSTRACT

Lips are a visible body part at the mouth of humans and many animals. Lips are soft, movable, and serve as the opening for food intake and in the articulation of sound and speech. Human lips are a tactile sensory organ, most of the substance of each lip is supplied by the orbicularis oris muscle, which encircles the opening. This muscle and others that radiate out into the cheeks make possible the lips' many variations in shape and expression. Lips are unique -- they aren't like any other part of the human body. But although they look different from the rest of your skin, they're actually quite similar. The lips form the border between the exterior skin of the face and the mucous membranes of the interior of the mouth. The skin of the lips has no hair follicles, no sweat glands and no sebaceous glands. Because of this, there is no production of natural emollients or perspiration to keep the skin smooth, and the thinness means that the lips can become dry and chapped easily. The thinness of the lips also means that the blood vessels below the surface are more readily visible and in individuals who have pale skin tone, the lips have much fewer melanocytes (pigment cells) and often take on a very pink tone. With individuals of darker skin tone, the lips are often less notably different in color. Lip drug administration can be used to deliver drugs for either local or systemic effect. The review highlights on the anatomy and physiology of lips, various diseases affecting them, its formulations and the treatment options as novel drug delivery platform.

Keywords: Translabial drug delivery, systemic route, lip skin,

INTRODUCTION

In human anatomy, the mouth is the first portion of the alimentary canal that receives food and saliva. In addition to the primary role as the beginning of the digestive system, mouth also plays a significant role of communication. It consists of two regions, the vestibule and the oral cavity proper. The mouth is lined by stratified squamous epithelium, from which oral smears may be taken for chromosomal studies. The oral cavity consists of two portions, the vestibule and the oral cavity proper. The vestibule is the cleft between the lips and cheeks externally and the gums and teeth internally. The parotid duct opens opposite the upper second molar. The oral cavity proper is bounded by the alveolar arches, teeth and gums, and palate and tongue. The submandibular duct opens on an elevation, the sublingual papilla, on the sides of the frenulum. Laterally, the sublingual fold, which is produced by the sublingual gland, contains the openings of the sublingual ducts. Light microscopy reveals several distinct patterns of maturation in the epithelium of the human oral mucosa based on various regions of the oral cavity.(14) Three distinctive layers of the oral mucosa are the epithelium, basement membrane, and connective tissues. The oral cavity is lined with the epithelium, below which lies the supporting basement membrane which in turn is supported by connective tissues.

The epithelium, as a protective layer for the tissues beneath, is divided into (a) non-keratinized surface in the mucosal lining of the soft palate, the ventral surface of the tongue, the floor of the mouth, alveolar mucosa, vestibule, lips, and cheeks, and (b) keratinized epithelium which is found in the hard palate and non-flexible regions of the oral cavity. The buccal epithelium is classified as a non-keratinized tissue. The term 'buccal', even if is used wrongly to indicate the mucosa of the total oral cavity, refers to the lining of the cheek and the upper and lower lips,

which represent one-third of the total oral mucosal surface (Figure : 1) . **Lips** are fleshy folds lined externally by skin and internally by mucus membrane and it bounds the oral fissure. The upper and lower lips are referred to as the "Labium superius oris" and "Labium inferius oris" respectively. The junction where the lips meet the surrounding skin of the mouth area is the vermilion border and the typically reddish area within the borders is called the vermilion zone.(17) The mucocutaneous junction lies at the edge of lip are red partly because the skin translucent and partly of the vascular papillae or thelia are unusually long where the mucosal surface is seen. The vermilion border of the upper lip is known as the cupid's bow. The fleshy protuberance located in the center of the upper lip is a tubercle known by various terms including the procheilon (also spelled prochilon), the "tuberculum labii superioris", and the "labial tubercle". The vertical groove extending from the procheilon to the nasal septum is called the philtrum. The skin of the lip, with three to five cellular layers, is very thin compared to typical face skin, which has up to sixteen layers. With light skin color, the lip skin contains fewer melanocytes (cells which produce melanin pigment, which give skin its colour). Because of this, the blood vessels appear through the skin of the lips, which leads to their notable red coloring. The skin of the lip forms the border between the exterior skin of the face, and the interior mucous membrane of the inside of the mouth. Buccal and mandibular branches of facial nerve supply to lips. These nerve innervations compress the lips together. Profuse bleeding of the lips can be controlled by compressing the labial arteries between the point of hemorrhage and the corner of the mouth. Pulsation of the superior and inferior labial arteries between the labial musculature and the glandular epithelium of the lip mucosa can be felt. Small nodular labial glands are present across the back of lower and upper lips. The fibers encircle the oral orifice within the substance of the lips. Some of the fibers arise near the midline from the maxilla above and the mandible below . Other fibers arise from the deep surface of the skin and pass obliquely to the mucous membrane(18). Many of the fibers are derived from the buccinator muscle. There are various differences between regular skin and lip skin.(Figure 2) The lip skin is not hairy and does not have sweat glands. Therefore it does not have the usual protection layer of sweat and body oils which keep the skin smooth, inhibit pathogens, and regulate warmth. For these reasons, the lips dry out faster and become chapped more easily. (Figure 3)

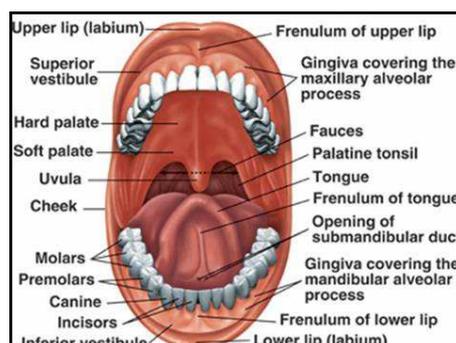


Figure 1: Labeled diagram of Oral cavity

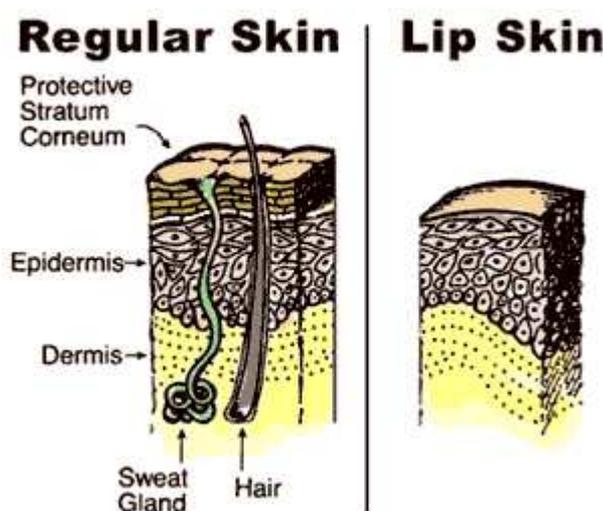


Figure 2 : Comparison between regular skin and normal skin

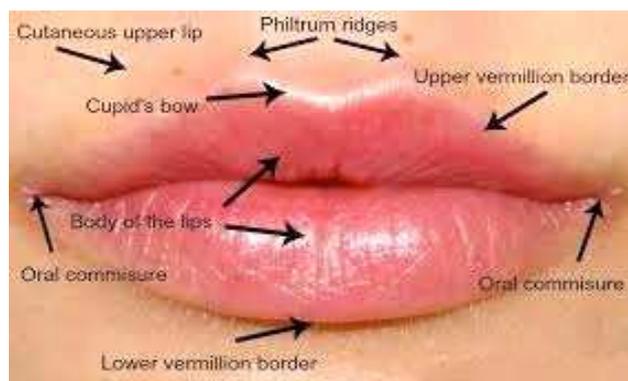


Figure 3: Anatomy of Lips

Histology

The skin of the lips is stratified squamous epithelium. The mucous membrane is represented by a large area in the sensory cortex, and is therefore highly sensitive. The Frenulum Labii Inferioris is the frenulum of the lower lip. The Frenulum Labii Superioris is the frenulum of the upper lip.(Figure : 4)

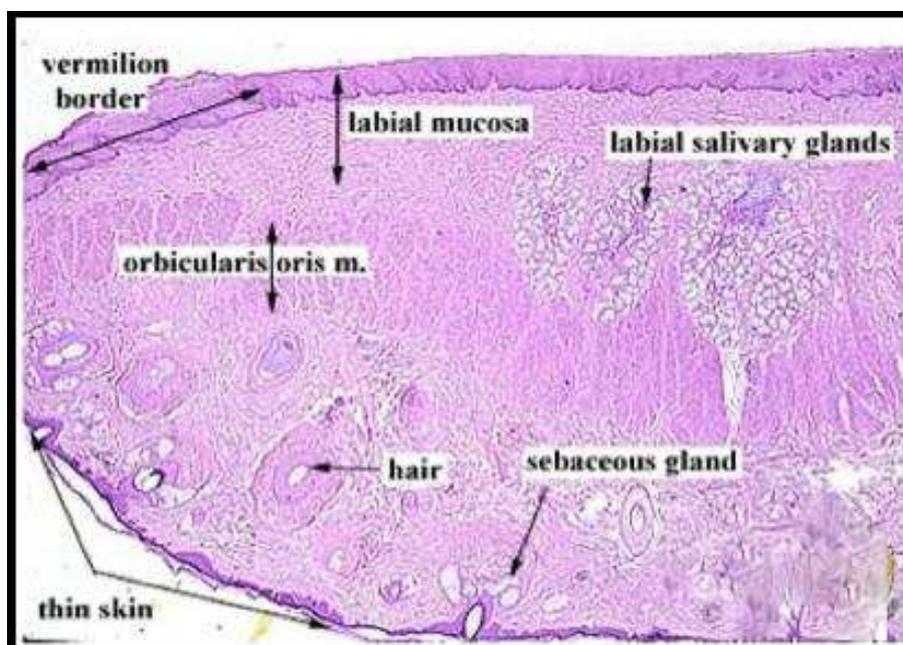


Figure :4 Histology of Lips

Innervation

Trigeminal nerve

1. The infra orbital nerve is a branch of the maxillary branch. It supplies not only the upper lip, but much of the skin of the face between the upper lip and the lower eyelid, except for the bridge of the nose.
2. The mental nerve is a branch of the mandibular branch (via the inferior alveolar nerve). It supplies the skin and mucous membrane of the lower lip and labial gingiva (gum) anteriorly.

Blood supply-The facial artery is one of the six non-terminal branches of the external carotid artery. It supplies the lips by its superior and inferior labial branches, each of which bifurcate and anastomose with their companion artery from the other side.

Muscles-The muscles acting on the lips are considered part of the muscles of facial expression. All muscles of facial expression are derived from the mesoderm of the second pharyngeal arch, and are therefore supplied (motor supply) by the nerve of the second pharyngeal arch, the facial nerve (7th cranial nerve). The muscles of facial expression are all specialized members of the panniculus carnosus, which attach to the dermis and so wrinkle, or dimple the overlying skin. Functionally, the muscles of facial expression are arranged in groups around the orbits, nose and mouth.

The muscles acting on the lips:

- Sphincters of the oral orifice
- Buccinator
- Orbicularis oris
- Anchor point for several muscles
- Modiolus
- Lip elevation
- Levator labii superioris
- levator labii superioris alaeque nasi
- Levator anguli oris
- Zygomaticus minor
- Zygomaticus major
- Lip depression
- Risorius
- Depressor anguli oris
- Depressor labii inferioris
- Mentalis

Functions

Because they have their own muscles and bordering muscles, the lips are easily movable. Lips are used for eating functions, like holding food or to get it in the mouth. In addition, lips serve to close the mouth airtight shut, to hold food and drink inside, and to keep out unwanted objects. Through making a narrow funnel with the lips, the suction of the mouth is increased. This suction is essential for babies to breast feed. Lips can also be used to suck in other contexts, such as sucking on a straw to drink liquids.

Articulation-The lips serve for creating different sounds mainly labial, bilabial, and labiodental consonant sounds as well as vowel rounding and thus are an important part of the speech apparatus. The lips enable whistling and the performing of wind instruments such as the trumpet, clarinet, flute and saxophone.

Tactile organ-The lip has many nerve endings and reacts as part of the tactile (touch) senses. Lips are very sensitive to touch, warmth, and cold. It is therefore an important aid for exploring unknown objects for babies and toddlers.

SIGNS OF LIP PROBLEMS

Lip symptoms include lip dryness, cracking, pain, numbness, sores and swelling. If lip pain is present, it may be described as sharp, dull, stabbing, burning or throbbing. Also experience lip symptoms as a result of injury, such as biting your lips or burning them with hot food. In other cases, your lip symptoms may be related to a chronic medical condition, such as anemia or infection with herpes simplex virus. Even a common infection can cause lip symptoms. Diseases or conditions that affect the nerves and muscles, including nerve damage or neuropathy, can be associated with symptoms that involve the lips. Lip symptoms may also be the result of cold and dry weather, infection, nutritional deficiencies, or medication side effects. A rare but potentially life-threatening cause of lip symptoms is cancer.

SYMPTOMS

Lip symptoms may accompany other symptoms affecting the mouth including Bleeding or bruising, Burning feeling, Cracked lips or mouth corners, Development of small bumps or blisters, Dry mouth, Hoarse voice, Itchy feeling, Pins-and-needles (prickling) sensation, Redness, warmth or swelling, Tenderness, Tingling or other unusual sensations.

CAUSES

1. Environmental causes of lip symptoms may be caused by environmental conditions including Cold weather, Dry weather, Sun damage, Wind exposure
2. Neuropathic causes of lip symptoms such as numbness may also result from neuropathy, a disorder of or damage to the nerves. In the case of lip symptoms, the nerves cannot carry a signal between the lips and the brain, causing numbness and sometimes a loss of control. Causes of lip symptoms due to neuropathy include Alcohol abuse, Cancer, Exposure to toxic chemicals, Guillain-Barré syndrome (autoimmune nerve disorder),Hypothyroidism (underactive thyroid),Ischemia (insufficient flow of blood to the lips),Lyme disease (bacterial infection spread by tick bites),Multiple sclerosis (disease that affects the brain and spinal cord causing weakness, coordination, balance difficulties, and other problems),Vitamin B12 deficiency (as in pernicious anemia)

3. Traumatic causes of Lip symptoms may also be due to injuries resulting from Biting your lips, Braces, poorly fitting dentures, or other physical irritants, Breathing through the mouth, Burns, Cuts, Head injury, Hot food and beverages, Repeated licking of the lips.

4. Other types of chronic diseases and conditions can lead to lip symptoms. These disorders include Iron deficiency anemia (low red blood cell count), Autoimmune disorders, Common cold (viral respiratory infection), Dermatitis (rash), Hemophilia (rare hereditary disorder in which blood does not clot normally) or other bleeding disorders, Herpes simplex virus infection, Malnutrition, Vitamin deficiency (including vitamins A, B12, C and folate), Weakened immune system

5. Serious or life-threatening causes lip symptoms that should be immediately evaluated in an emergency setting. These include Anaphylaxis (life-threatening allergic reaction), Cancer, Dehydration (loss of body fluids and electrolytes, which can be life threatening when severe and untreated), Hyperventilation, Medication side effects, Severe infection, Toxic ingestion, such as eating poisonous plants, mushrooms or chemicals.

The potential complications of lip symptoms

Brain damage, Impaired balance and coordination, Nerve problems that cause pain, numbness or tingling, Organ failure or dysfunction, Severe discomfort or pain, Skin ulcerations and infections, Spread of cancer, Spread of infection, Vitamin deficiencies.(1)

LIP DISEASES

The lips are a prominent part of the face, and a rash or sore here can be difficult to ignore and hide. Cold sores (orofacial herpes) are a common viral infection that involve the lips.(2)

ACTINIC CHEILITIS

Actinic cheilitis is a precancerous condition related to cumulative lifetime sun exposure. The lower lip is most often affected. They will frequently exhibit other effects of sun-damaged skin, such as precancerous lesions on the skin called actinic keratoses and extensive wrinkling. A certain type of skin cancer (squamous cell carcinoma) develops in 6–10% of cases of actinic cheilitis. Actinic cheilitis is significantly more common in men, the elderly, and fair-skinned individuals. There is also a strong association with tobacco use. The major signs and symptoms include persistent redness, scaliness, and chapping are among the symptoms noted. Erosions and cracks (fissures) may be present as well. It is located on the lips, most often the lower lip. Wearing barrier clothing (eg, wide-brimmed hats) and sunscreen-containing lip balms can aid in preventing actinic cheilitis. The medical care is need to be sought when persistent scaling of the lips is noted. A biopsy of the lip may be needed to rule out squamous cell carcinoma.

ACTINIC KERATOSES

Actinic keratoses, also known as solar keratoses (senile keratosis), are small rough or scaly areas of skin due to damage from sun exposure. Some actinic keratoses can turn into squamous cell skin cancer. People with fair skin who sunburn easily; have trouble tanning; have blue, green, or hazel eyes; and red or blond hair are most at risk for developing actinic keratoses. Darker-skinned individuals are rarely affected. The signs and symptoms include the sun-exposed areas of the face, scalp (where balding), ears, neck, forearms, and backs of the hands are most commonly affected with actinic keratoses, but any skin area frequently exposed to sun can be involved. Patches are usually less than an inch in size with slight scale (sometimes thick like a wart) and a pink, red, or brownish color. They are slightly rough to the touch, like fine sandpaper, and may be a bit sensitive (Table 1).

- Mild – one or two spots, not thick or hard
- Moderate – scattered, few spots
- Severe – numerous or thick, hard, or bleeding spots

Table 1: Treatment option for Actinic keratoses(9)

MEDICATION	PROCEDURES	PREVENTION
Fluorouracil cream	Cryotherapy	Limiting extent of sun exposure
Imiquimod cream	Photodynamic therapy	Using sun protection
Ingenol mebutate gel	Chemical peeling	
Diclofenac sodium gel	Laser therapy	
Retinoids	Surgical techniques	
	<ul style="list-style-type: none"> • Surgical excision • Shave excision • Dermabrasion 	

ANGULAR CHEILITIS

Angular cheilitis (perlèche) is a chronic inflammatory condition of the corners of the mouth. Usually associated with a fungal (*Candida*) or bacterial (*Staphylococcal*) infection. Multiple local and systemic predisposing factors are involved in the initiation and persistence of lesion. Such factors include nutritional deficiencies, over closure of the mouth, a lip-licking habit, chronic pooling of saliva (drooling) and patients who are immunocompromised, have undergone head and neck radiation, or have diabetes mellitus are also prone to this condition.

Treatments

Treatment of angular cheilitis is usually undertaken with topical antifungals such as nystatin, clotrimazole, or econazole. Combinations of a topical antifungal and a topical steroid – such as Mycostatin® and triamcinolone or iodoquinol and hydrocortisone may also be prescribed. In persistent cases, oral antifungals may be used to treat the condition.

CHAPPED LIPS(CHEILITIS)

Chapped lips (cheilitis) are lips that appear dry, scaly, and may have one or more small cracks. Retinoids (isotretinoin and acitretin) are the most frequent drug-induced causes for chapped lips. Other drugs reported to have induced chapped lips include:

- High doses of vitamin A
- Lithium
- Chemotherapeutic agents (busulfan and actinomycin)
- D-penicillamine
- Isoniazid
- Phenothiazine

Other possible causes of chapped lips include high fevers as well as environmental conditions, such as cold weather, dehydration, and certain vitamin deficiencies.

Caution

- Avoid lip licking because since this may worsen the condition.
- Avoid "medicated" lip preparations because they increase the risk of developing an allergic reaction.

Lip-licking cheilitis is best treated with avoidance of the licking behavior. Drug-induced cheilitis is treated with avoidance of the offending drug.

COLD SORES(OROFACIAL HERPES)

Herpes simplex virus type 1 (HSV-1) is the cause of oral infection. Herpes simplex infection of the mouth and face, known as orofacial herpes simplex, herpes labialis, cold sores, or fever blisters, is a common, recurrent skin condition associated with infection by the herpes simplex virus (HSV). Orofacial HSV usually appears as small blisters or sores around the mouth, nose, genitals, and buttocks, though infections can develop almost anywhere on the skin. Infections with HSV are very contagious and are spread by direct contact with the skin lesions. There are 2 types of HSV: herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 (HSV-2). HSV-1 infections usually occur around the mouth, lips, nose, or face, while HSV-2 infections usually involve the genitals or buttocks. However, HSV-1 can sometimes cause infections in the genitals or buttocks, while HSV-2 can occasionally cause infections around the mouth, lips, nose, or face. However, only about 20% of people who are infected with HSV actually develop visible blisters or sores. Only 20% of people who are infected with HSV actually develop visible blisters or sores. That means that approximately 80% of people with HSV infections have not been diagnosed and are unaware of their condition.(3)

Risk factors

- Transmission is due to viral shedding into saliva and can occur by direct contact with saliva (eg, kissing). Viral shedding into saliva may occur during asymptomatic infection but it is thought that the risk of infection is much smaller than during symptomatic infection.
- Viral shedding can occur up to 60 hours after the onset of symptoms.
- Factors that may trigger a recurrence of oral herpes simplex include immunosuppression (eg, corticosteroids), upper respiratory tract infections, fatigue, emotional stress, physical trauma, exposure to sun (ultraviolet light), trauma and menstruation.
- Obesity may increase susceptibility to HSV-1 infection.(4)

Signs and Symptoms

The most common locations for HSV-1 infections include:

- Lips
- Mouth (including gums, tongue, roof of mouth, and inside the cheeks)
- Nose
- Chin
- Cheeks

Primary infection:

- This occurs most often in infancy or childhood. It may or may not be symptomatic.
- Gingivostomatitis is the most common presentation in young children. It presents with vesicles and ulcers on the tongue, lips, gums, buccal mucosa and hard and soft palates.
- Pharyngitis is a more common presentation in adolescents, with lesions in the throat associated with viral symptoms similar to those of glandular fever.
- Herpetic whitlow may occasionally occur via spread to the fingers.

Recurrent infection:

- Cold sore lesions are the most common form of recurrent disease. They tend to occur in the same location, be unilateral and recur two or three times a year on average.
- Prodromal symptoms may occur 6-24 hours before the appearance of a lesion and include tingling, pain and/or itching in the perioral area.
- Cold sores are usually seen on the lips and extend to the skin around the mouth. Other areas on the face, chin, or nose are sometimes involved. Lesions begin as erythematous areas that swell into papules. These become vesicles, which then collapse into ulcers. This takes 1-3 days. The ulcers crust over and the skin returns to normal within about two weeks.(5)

COMMON WART

Warts are growths of the skin and mucous membranes (the mouth or genitals) that are caused by over 100 types of the human papillomavirus (HPV). Common warts are usually found on areas of the body prone to trauma, such as the elbows, knees, and hands. The virus causes thickening of the top skin layer. They are usually painless and go away on their own, sometimes taking a few months to resolve, but can take up to two years. Warts are usually acquired from person-to-person contact. The virus is not highly contagious but can cause an infection by entering through a small break in the skin. In the same way, warts can be spread to other places on your own body. Warts can affect people of any age, but they are most common between the ages 12–16. It is estimated that 20% of schoolchildren and about 10% of the general population have warts. Those with HIV, organ transplants, or on chemotherapy have a higher incidence of warts due to their weakened immune system.

Signs and Symptoms

- Warts may occur singly or in multiples and often have multiple small black "dots" at the surface from tiny blood vessels. Common warts are rough, thick, skin-colored, pink, or white bumps from 1 mm to over 10 mm in size, often on the hands, face, elbows, and knees.
- Filiform warts are long and narrow, like tufts of thread, and usually small at the base (1–3 mm); they often affect the face, eyelids, or nose area.
- Flat warts are very slightly raised, smooth, 1–5 mm, skin-colored bumps that may appear in a line from self-inoculation from scratching or widely from shaving. They are often seen on the face, hands, or shins.
- Plantar warts are thick, rough, callus-like, often tender areas of the soles of the feet, usually on the weight-bearing areas. Since they are painful, they are often thought to be corns.

Wart infection can be described as:

- Mild – just one or a few painless lesions
- Moderate – 10–20 lesions that are painless
- Severe – pain that limits normal life activities, bleeding, or over 20 lesions, except for flat warts, which can be numerous, yet not bothersome.

FORDYCE SPOTS

Fordyce spots are normal large, superficial sebaceous (oil-producing) glands seen on the moist tissue that lines some organs and body cavities (mucosal surfaces). The "spots" are asymptomatic and can be found on the head of the penis, the inner foreskin, and, most commonly, at the border of the lips. These sebaceous glands are not associated with hair follicles. These lesions are asymptomatic, but itching or irritation may occur if people treat the bumps inappropriately.

Fordyce spots can appear at any point in life, but the incidence of appearance increases with age, with the largest prevalence in elderly patients.

Signs and Symptoms

- The most common location for Fordyce spots is at the border of the lips, especially near the corners of the mouth. Other locations include the back portions of the inner cheeks and inside the mouth, including the tonsils. The head of the penis and inner portion of the foreskin may be affected as well.
- Multiple (usually less than 10) 1–2 mm, painless, yellowish papules are seen.

Treatment

Mild topical steroids provide relief.

KERATOCANTHOMA

Keratoacanthoma (KA) is a rapidly growing skin cancer usually appearing as a volcano-like bump on the sun-exposed skin of middle-aged and elderly individuals. Many scientists consider keratoacanthoma to be a less serious form of squamous cell carcinoma. Most keratoacanthoma cause only minimal skin destruction, but a few behave more aggressively and can spread to lymph nodes.

Risk factors for the development of keratoacanthoma include:

- Age over 50
- Fair skin, light hair, or light eyes
- Male
- Chronic exposure to sunlight or other ultraviolet light
- Exposure to certain chemicals, such as tar
- Exposure to radiation, such as X-ray treatment for internal cancers
- Long-term suppression of the immune system, such as organ transplant recipients
- Long-term presence of scars, such as from a gasoline burn
- Chronic ulcers
- Presence of particular strains of the wart virus (human papillomavirus)
- Previous skin cancer

Signs and Symptoms

The most common locations for keratoacanthoma include:

- Center of the face
- Backs of hands
- Forearms
- Ears
- Scalp
- Lower legs, especially in women

Treatments

Diagnosis by skin biopsy.

LICHEN PLANUS

Lichen planus (LP) is a disease of the skin and, less often, the scalp, fingernails, toenails, and/or inside the mouth or genitalia (mucous membranes). Lichen planus can resolve on its own without treatment or be chronic, even with aggressive treatment. The cause of the inflammation that leads to lichen planus is unknown. People of all ages, of all races, and of both sexes can have lichen planus. However, it is rarely seen in young children and older adults, most commonly occurring in people aged 30-60. Although the cause of lichen planus is unknown, some people with the condition also have hepatitis C, an infection of the liver. People who take certain medications may develop a rash that looks like lichen planus (drug-induced lichen planus). These medications include:

- High blood pressure (hypertension) medicines, including diuretics, ACE inhibitors, and calcium channel blockers
- Diabetes medications, including the sulfonylureas
- Ibuprofen or naproxen
- Antimalarial medications
- Gold
- Penicillamine
- Ketoconazole

Signs and Symptoms

The most common locations for lichen planus include:

- Inner wrists
- Forearms
- Inner ankles
- Lower legs
- Neck
- Trunk
- Inside the mouth
- Fingernails and toenails
- Scalp
- Genitals

Treatments

Diagnosis by skin biopsy.

- Topical corticosteroid (cortisone) cream, lotion, ointment, or gel
- Topical tacrolimus or pimecrolimus
- Anti-itch lotions containing menthol, pramoxine, or phenol
- Corticosteroid (cortisone) injected directly into a thick lesion
- Oral antihistamine pills such as diphenhydramine, loratadine, cetirizine, fexofenadine, desloratadine, or hydroxyzine for itching

In addition, your doctor may suggest one of the following treatments for oral lichen planus:

- Topical corticosteroid (cortisone) ointment or gel
- Topical cyclosporine solution used as a mouthwash

For very severe cases of lichen planus, one of the following therapies may be recommended:

- Ultraviolet light treatment
- Oral retinoid pills such as isotretinoin or acitretin
- Oral cyclosporine pills
- Oral hydroxychloroquine pills

MELASMA

Melasma is a common disorder of unknown cause that causes dark (hyperpigmented) patches, primarily on the face. The condition is marked by brown patches that worsen in response to increases of the hormone estrogen, such as during pregnancy or with the use of birth control pills. Other medications, such as anti-seizure medications, may also cause melasma..

Signs and Symptoms

The dark patches of melasma most commonly affect the face, particularly the sides (lateral portions) of the cheeks and sometimes the skin above the lips.

The most common locations for an oral melanotic macule include:

- Lips, especially the lower lip
- Gums (gingiva)
- Inner cheek (buccal mucosa)
- Roof of the mouth (hard or soft palate)

Treatments

- Use bleaching agents (hydroquinone 4%) carefully. Do not apply these agents to the normally pigmented surrounding skin, as normal skin may also be bleached. Use hydroquinone under the supervision of a physician, as side effects, such as darkening of the skin, may occur.
- Hydroquinone is often irritating and may require the use of 1% hydrocortisone cream, which may also help with the hyperpigmentation. Combination therapy with tretinoin cream may also be helpful.
- Superficial chemical peels (application of an acid to remove the top layers of the skin) and microdermabrasion (a facial sanding technique) may offer additional help.
- A topical agent, azelaic acid, may be helpful.
- Laser therapy has not yet been shown to be satisfactory treatment. Melasma may return and hyperpigmentation may develop in the treated area.

ORAL MELANOTIC MACULE

Oral melanotic macule is a non-cancerous (benign), dark spot found on the lips or inside the mouth. An oral melanotic macule found on the lip is sometimes called a labial melanotic macule. Oral melanotic macules can appear in people of any age, of any race, and of either sex. However, they are more common in middle-aged people, in dark-skinned people, and in females.

Signs and Symptoms

The most common locations for an oral melanotic macule include:

- Lips, especially the lower lip
- Gums (gingiva)
- Inner cheek (buccal mucosa)
- Roof of the mouth (hard or soft palate)

Treatments

Diagnosis by a skin biopsy.

PERIORAL DERMATITIS

Perioral dermatitis is an acne-like condition of unknown cause. Some possible causes are the use of topical corticosteroid creams, cosmetic products, oral contraceptives, fluoride and anti-tartar ingredients in dental products, and it tends to occur in those prone to eczema. It is usually seen in women ages 16–45, but men can be affected as well. Children may also be affected (ages 7 months to 13 years). It is more common in developed countries.

Signs and Symptoms

Small red bumps or tiny pus-filled lesions (pustules) appear around the mouth, often with a clear area between the lip and the rash. The bumps may also occur near the eyes and nose. There may also be dry or flaky skin in these areas.

Treatments

Taking oral or topical antibiotics for a few weeks may provide effective treatment. Azelaic acid is a topical product that may be prescribed. Sometimes the condition recurs after treatment is stopped, but the same therapy may be repeated as needed.

PYOGENIC GRANULOMA

Pyogenic granuloma is a common, benign growth that often appears as a rapidly growing, bleeding bump on the skin or inside the mouth. It is composed of blood vessels and may occur at the site of minor injury. When a pyogenic granuloma occurs in a pregnant woman, it is sometimes called a "pregnancy tumor" (granuloma gravidarum). Pyogenic granulomas develop in up to 5% of pregnant women.

Signs and Symptoms

The most common locations for pyogenic granulomas include:

- Lips, gums, and inner mouth (particularly in pregnant women)
- Hands and fingers
- Head and neck
- Feet and toes
- Upper trunk

Treatments

Diagnosis by skin biopsy.

Although pyogenic granuloma is a benign condition, it is frequently removed due to its tendency to bleed, its tenderness, and its distressing appearance. However, untreated pyogenic granulomas may go away on their own. In obvious cases of pyogenic granuloma, your physician may choose to treat it immediately after obtaining the biopsy.

Such treatments include:

- Scraping and burning (curettage and cauterization). After numbing with local anesthetic, the area is scraped with a sharp instrument (a curette) and burned with an electric needle (cautery).
- Silver nitrate solution
- Topical imiquimod cream (Aldara®)
- Laser treatment
- Freezing with liquid nitrogen (cryotherapy)

- Surgical removal (excision)

SQUAMOUS CELL CARCINOMA

• Squamous cell carcinoma (SCC) is the second most common form of skin cancer. Squamous cell carcinoma usually occurs on sun-damaged skin, especially in light-skinned individuals with a long history of chronic sun exposure. Squamous cell carcinoma requires treatment to prevent it from becoming too invasive. If it is caught early and treated appropriately, squamous cell carcinoma rarely spreads (metastasizes) to lymph nodes or to internal organs.

Signs and Symptoms

The most common locations for squamous cell carcinoma in light-skinned individuals include:

- Head and neck
- Arms and hands
- Shoulders
- Back
- Lower lip, especially in smokers

Treatments

Diagnosis by performing a biopsy of the lesion.

- Cryosurgery with liquid nitrogen
- Electrodesiccation and curettage, also known as "scrape and burn"
- Excision
- Mohs micrographic surgery
- Radiation (10)

THRUSH ORAL CANDIDIASIS

Thrush (oral candidiasis), also known as oral moniliasis, is a yeast infection of the mouth or throat (the oral cavity). The yeast that most commonly causes oral candidiasis is *Candida albicans*.

Signs and Symptoms

Thrush may appear as white or pale yellow spots on the inner surfaces of the mouth and throat, the tongue, and the lips. It may resemble cottage cheese or milk curds. However, scraping off these membranes may be difficult and may leave slightly bleeding sores. Thrush may be associated with a burning sensation in the mouth or throat.

Treatments Although meticulous oral hygiene practices must be followed, treatments center on killing the overgrown yeast with anti-fungal medications.

- Nystatin – This medicine must come into contact with the yeast in order to kill it. Nystatin comes in a suspension, or liquid, and in a lozenge, also called a troche. The suspension is swished around the mouth and then swallowed. The lozenge dissolves in the mouth. Both the suspension and the lozenges are used several times a day until the lesions are completely gone.
- Amphotericin B suspension – The suspension is swished and swallowed several times a day until complete resolution of the lesions.
- Clotrimazole lozenge – The lozenge is dissolved in the mouth several times a day until the lesions have disappeared entirely.
- Fluconazole pill – This medication is swallowed once daily for 5–10 days.

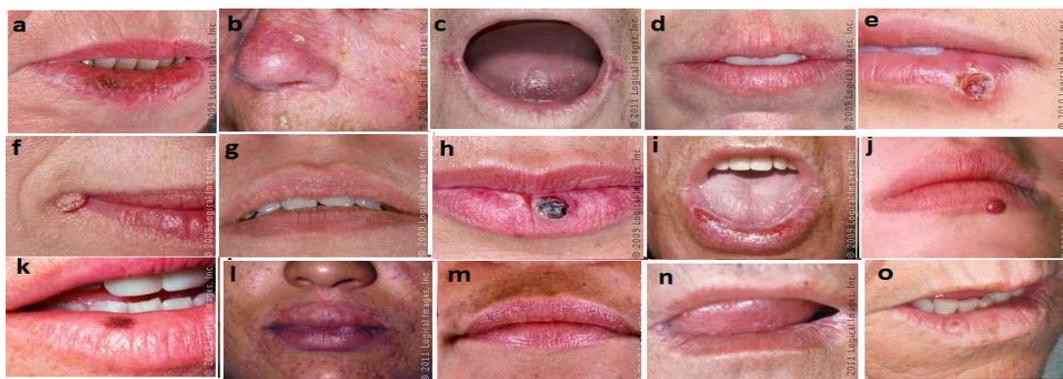


Figure shows:

- a) Actinic cheilitis
- b) Actinic keratoses
- c) Angular cheilitis
- d) Chapped lips
- e) Cold sores
- f) Common warts
- g) Fordyce spots
- h) Keratoacanthoma
- i) Lichen planus
- j) Melasma
- k) Oral Melanotic Macule
- l) Perioral dermatitis
- m) Pyogenic granuloma
- n) Squamous cell carcinoma
- o) Thrush (oral candidiasis)

LIP FORMULATIONS:

Lip balm

Lip balm or **lip salve** is a wax-like substance applied topically to the lips of the mouth to moisturize and relieve chapped or dry lips, angular cheilitis, stomatitis, or cold sores. Lip balm often contains beeswax or carnauba wax, camphor, cetyl alcohol, lanolin, paraffin, and petrolatum, among other ingredients. Some varieties contain dyes, flavor, fragrance, phenol, salicylic acid, and sunscreens. Lip balms are formulations applied onto the lips to prevent drying and protect against adverse environmental factors. Lip balm should not be considered equivalent to the lip gloss, with the former being a product intended for use by both men and women.

The main ingredients of lipstick (Table 2) are fatty acids, such as waxes, oils and butters, which provide consistency and work as emollients in the preparations. Among these, castor oil, beeswax, carnauba wax, candelilla wax, paraffin and cocoa butter are often used. Lipstick also contains additives, such as antioxidants, conservatives and fragrances, as well as dyes and pigments.

Table 2: Formulation of Lip Balm

INGREDIENTS	FUNCTIONS
Avobenzone 2.0%, Octocrylene 10.0%, Oxybenzone 6.0%	Sunscreen
Petrolatum, Polyethylene, Microcrystalline Wax, Theobroma Cacao (Cocoa) Seed Butter, Silica Tocopheryl Acetate, Ascorbic Acid, Retinyl Palmitate	Base/Structuring Agents Antioxidants/ Vitamins
Sodium Saccharin, Flavor	Sweetening /flavor
Propylparaben, Butylparaben Ethylhexyl Palmitate, Trimethylsiloxyphenyl Dimethicone, Isopropyl Myristate, PEG-8, Aloe Barbadensis Leaf Extract, Caprylyl Glycol	Preservatives Skin Conditionings /Emollients /Humectants

The primary purpose of lip balm is to provide an occlusive layer on the lip surface to seal moisture in lips and protect them from external exposure. Dry air, cold temperatures, and wind all have a drying effect on skin by drawing moisture away from the body. Lips are particularly vulnerable because the skin is so thin, and thus they are often the first to present signs of dryness. Occlusive materials like waxes and petroleum jelly prevent moisture loss and maintain lip comfort while flavorants, colorants, sunscreens, and various medicaments can provide additional, specific benefits.

Lip balm can be applied where a finger is used to apply it to the lips, or in a lipstick-style tube from which it can be applied directly.(11)

LIPSTICK (12,13)

The details are given in Table 3.

Table 3: Formulation of Lip Stick

INGREDIENTS	EXAMPLES
Wax	Bees wax, Ozokerite, Candelilla wax, Carnauba wax
Oils and fats	Olive oil, Mineral oil, Cocoa butter, Lanolin , Petrolatum, Pig fat, Castor oil
Antioxidants	BHT, BHA, Propyl gallate , Citric acid
Emollients	Ointments , Creams , Lotions
Pigments and Dyes	Bromo acid, D&C Red No. 21, D&C Red 7, D&C Red 34 ,D&C Orange No. 17

TYPES

- Matte lipstick
- Crème lipstick
- Glossy lipstick
- Shimmery lipstick

LIP STAIN

Lip stain is a cosmetic product used to colour the lips, usually in form of aliquid or gel. It generally stays on longer than lipstick by leaving a stain of colour on lips.

LIP GLOSS

Lip gloss is a product used primarily to give lips glossy luster and sometimes to add a subtle colour. It is distributed as a liquid or a soft solid unlike lip balm which generally has medicinal or soothing purposes. The product is available in ranges of opacity and translucent to solid, and can have various frosted, glittered, glossy and metallic finish.

LIP LINER

Lip liner is also known as lip pencil which is used outline the lips. The product is usually sold in a retractable tube or pencil form. Lip liner is usually available in the same range of colours as lipsticks. Lip liner also comes in invisible, for giving the illusion of smooth lips without adding or affecting colour.(19,20)

CONCLUSION

Different to facial skin, the lip skin is more delicate and very sensitive to the outside environment. A routinely protection with moisturizing lip care products helps in maintaining our lips a healthy look and feeling of well being. The local permeability of the labial mucosa can be enhanced by designing of suitable formulations as well as a novel strategic drug delivery approach.

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