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Pentoxifylline in Dermatology: Mechanisms of Action, Clinical Applications, and Emerging Therapeutic Perspectives

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Abstract:

Background: Pentoxifylline (PTX) is a methylxanthine derivative and nonselective phosphodiesterase inhibitor originally introduced for peripheral vascular disease and intermittent claudication. Its ability to improve erythrocyte deformability, reduce blood viscosity and platelet aggregation, enhance microcirculatory flow, and modulate inflammatory and fibrotic pathways has encouraged its use in dermatology. PTX increases intracellular cyclic adenosine monophosphate and suppresses tumor necrosis factor alpha and other proinflammatory cytokines, while reducing leukocyte adhesion, oxidative stress, fibroblast proliferation, and extracellular matrix production. These combined hemorheological, anti-inflammatory, immunomodulatory, and antifibrotic actions provide a rationale for its application in disorders characterized by vascular compromise, chronic inflammation, or excessive fibrosis. Reported dermatological indications include venous leg ulcers, livedoid vasculopathy, pigmented purpuric dermatoses, Behçet disease, leprosy reactions, psoriasis, graft-versus-host disease, sarcoidosis, actinic prurigo, alopecia areata, lipodermatosclerosis, necrobiosis lipoidica, pretibial myxedema, keloids, hypertrophic scars, morphea, and systemic sclerosis. PTX has also been evaluated as adjunctive therapy in leishmaniasis, oral submucous fibrosis, radiation-induced fibrosis, Stevens-Johnson syndrome, and toxic epidermal necrolysis. Although generally well tolerated and inexpensive, evidence varies considerably between indications, and many applications rely on small studies or case reports. Further controlled trials are required to establish optimal dosing, long-term safety, and comparative clinical effectiveness across diverse dermatological populations and clinical practice settings.

Keywords: Pentoxifylline; Dermatology; Phosphodiesterase inhibitor; Hemorheology; Tumor necrosis factor-alpha; Inflammation; Fibrosis; Microcirculation.

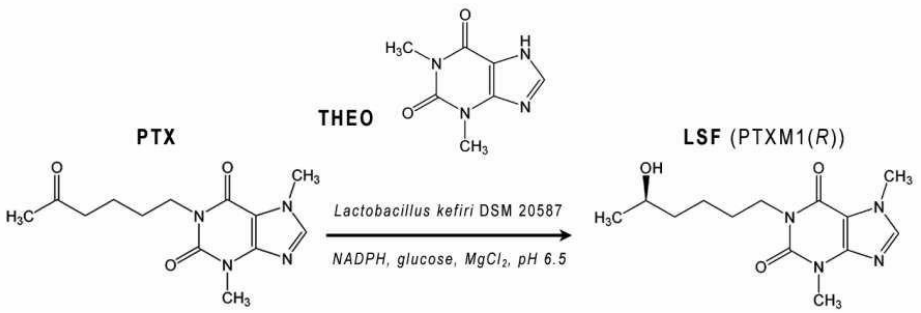
Introduction:

Pentoxifylline (PTX) or oxpentifylline is an analogue of the methylxanthine theobromine, which is known as a hemorrheologic agent due to its effect on red blood cells.It is a non-selective inhibitor of phosphodiestrases; primarily used in microcirculatory disorders **(1)**.

It is a dimethylxanthine-derivative with diverse pharmacological properties having a variety of anti-inflammatory and physiological effects at the cellular level, which may be important in treating a wide range of skin conditions, mostly as adjuvant therapy with beneficial effects **(2).**

Chemical Structure

Systematic International Union of Pure and Applied Chemistry name of pentoxifylline is 3,7-dimethyl-1- (5-oxohexyl)-3,7-dihydro- 1H-purine-2,6dione and its chemical formula is C13H18N4O3 **(3).** The structure is shown below



Pentoxifylline structure **(3)**

Pharmacokinetics and metabolism

After oral administration, the aqueous solution of PTX is almost completely absorbed. It undergoes first-pass metabolism and various metabolites appear in plasma very soon after administration; peak plasma levels reach within 2 hours. The major metabolites are metabolite I [1-(5hydroxyhexyl)-3,7-dimethylxanthine] and metabolite V [1-(3-carboxypropyl) -3,7-dimethylxanthine]. The plasma levels of these metabolites are respectively 5 and 8 times greater than PTX. Excretion is almost totally through urine, the main bio-transformation product being metabolite V and essentially no parent drug is found in urine. Despite variations in the levels of the parent compound and its metabolites in plasma, urinary recovery of metabolite V is consistent and dose proportional. Less than 4% of the administered dose is recovered in feces **(3).**

Topical forms of PTX have been studied aiming to treat skin diseases. A pharmacokinetic study of transdermal absorption of PTX has been applied in rats aiming to increase PTX bioavailability and sustain its release **(4).**

Mechanisms of action of PTX:

There are many hypotheses regarding the mechanism of action of PTX and its cellular and molecular effects, based on human and animal studies. This includes effects on immune modulation, anti-tumor necrosis factor-α (TNF-α) effects, hemorheological effects, anti-fibrinolytic effects, along with effects on endothelial cells and adhesion molecules **(3).**

1- Immune modulation

Pentoxifylline affects immune modulation by means of increased leukocyte deformability and chemotaxis, decreased endothelial leukocyte adhesion, decreased neutrophil degranulation and release of superoxides, decreased production of monocyte-derived TNF, decreased leukocyte responsiveness to interleukin 1 (IL-1) and TNF, inhibition of T and B lymphocyte activation and decreased natural killer cell activity **(3).**

2- Anti-TNF-α effects

Pentoxifylline is known to inhibit the production of TNF-α, which is an important inflammatory mediator with a wide spectrum of activity, predominantly produced by mononuclear cells. Increasing evidence has implicated TNF-α as a pivotal molecule involved in the pathogenesis of a wide variety of acute and chronic inflammatory disease states including many skin diseases such as psoriasis, graft-versus-host-disease (GVHD), contact dermatitis, and leprosy reactions **(2).**

Pentoxifylline is also an active inhibitor of already formed TNF. There is also evidence that PTX may influence other inflammatory cytokines, such as inhibition of IL-1 and IL-6 **(5).**

3- Hemorheological effects

Pentoxifylline affects almost all factors responsible for blood viscosity and is among the first known hemorheologically active drug. The primary hemorrheological effects of PTX are caused by increased red blood cell deformability and decreased blood viscosity. The possible mechanism by which this is achieved involves increased erythrocyte adenosine triphosphate and other cyclic nucleotide levels. Pentoxifylline leads to the inhibition of thromboxane and increase of prostacyclin synthesis. Hypercoagulability states improve because of

decreased platelet aggregation and adhesion; increased plasminogen activator, plasmin, and anti-thrombin III; decreased fibrinogen, alpha 2-antiplasmin, alpha-1 antitrypsin, and alpha2 macroglobulin. Furthermore, PTX increases leukocyte deformability, inferring the possibility of a greater role of polymorphonuclear leukocytes in whole blood viscosity. Thus, it can be considered as an almost complete rheological drug **(6)**.

4- Anti-fibrinolytic effects

Pentoxifylline increases fibroblast collagenases and decreases the production of collagen, fibronectin, and glycosaminoglycan. These effects could be attributed to its anti-TNFα properties or separate mechanisms as suggested by various studies **(7)** .

5- Other effects

Pentoxifylline is a non-selective inhibitor of cyclic-3', 5'-phosphodiesterase, leading to a broad-spectrum effect against cell proliferation and inflammation. It also reduces the expression of adhesion molecules such as intercellular adhesion molecule-I (ICAM-I) on keratinocytes and E-selectin expression on endothelial cells **(8)**.

Clinical applications of PTX In dermatology:

Pentoxifylline has found a place in the management of a variety of dermatological conditions. The following are the most common ones

- **Peripheral vascular diseases**

Pentoxifylline has been used world-wide for the treatment of intermittent claudication and in 1984 United States FDA approved its use for intermittent claudication in the United States. It has been marketed in Europe since 1972 for this purpose **(3).**

Various studies have shown the therapeutic efficacy of PTX in a significant percentage of patients with peripheral vascular disease.However, use in intermittent claudication still remains the main indication. Intravenous PTX may be of benefit in acute ischemic lesions in systemic sclerosis, when used as 1200 mg/day for 21 days. However, further studies are required to confirm these initial findings **(3).**

- **Vasculopathies and vasculitides**

Due to its multiple effects on various blood cells and probably through through its anti-inflammatory effects, PTX could be a useful drug in treating vasculopathies as described in various studies. Indeed, several studies have shown the beneficial effects of PTX in idiopathic livedoid vasculopathies and some authors suggest it as a drug of choice for this condition **(2).**

Cutaneous vasculitides are usually managed primarily with colchicine, dapsone, and prednisone. Theoretically, PTX can act as a sparing agent in different kinds of vasculitides, both through its extensive hemorheologic effects and also by neutralizing proinflammatory cytokines. Specifically, it seems that PTX works synergistically with dapsone in treating hypocomplementemic urticarial vasculitis **(9).**

- **Venous leg diseases and ulcers**

Pentoxifylline is also used in the treatment of venous leg disease and venous ulcers, especially in patients unable to tolerate compression therapy **(9).**

Histological and immunocytochemical analyses of venous leg ulcers suggest that inflammatory reactions play a great role in these ulcers. These inflammatory reactions lead to fibrosclerotic remodeling of the skin and then to ulceration. The leukocyte activation is accompanied by the expression of integrins and by the synthesis and release of many inflammatory molecules, including proteolytic enzymes, leukotrienes, prostaglandin, bradykinin, free oxygen radicals, cytokines, and possibly other classes of inflammatory mediators. As leukocytes become activated, they become rigid and immobile; this leads to further occlusion of small vessels and trophic changes in the overlying skin. The attention of many investigators has been drawn to the use of PTX as an adjunctive therapy

in venous leg ulcers. A systematic review has shown that PTX with compression is more effective than placebo with compression in patients with venous leg ulcers **(2).**

Pigmented purpuric dermatoses (PPD)

Successful treatment with pentoxifylline causes a decrease in the expression of ICAM-I on endothelial cells in and around PPD lesions, resulting in decreased exudation of inflammatory cells from capillaries into the surrounding perivascular tissue and reduced TNF mediated extravasations. Pentoxifylline, being economical, easily available, and devoid of serious side effects should be considered for use in Schamberg's disease, a type of PPD; some advocate it as first-line therapy. Although there is limited evidence, one study of three cases of Schamberg's disease revealed successful treatment with PTX. The authors suggested that PTX acts through its effects on adhesion molecules in this disease **(10).**

- **Aphthosis and Behçet disease**

Pentoxifylline has been found effective in recurrent oral and genital aphthosis. These beneficial effects may be due to anti-TNF-α properties of PTX as well as correction of impaired erythrocyte deformability, which is decreased in active behçet disease patients in comparison with healthy control subjects **(11).**

Furthermore, PTX has been used by many rheumatologists for the treatment of behçet disease. Pentoxifylline reduces the severity and duration of the symptoms. Hence, the therapeutic mechanism underlying the beneficial effect of PTX in behçet disease is possibly the correction of impaired erythrocyte deformability. Pentoxifylline can be also regarded as a preventive modality for thrombotic events, which are among the other characteristics of. *Behçet* disease **(11).**

- **Leprosy**

An increase in TNF-α has been implicated in type II leprosy reaction. Several studies have been documented that PTX rapidly ameliorates the systemic symptoms of type II leprosy reaction and could be an ideal alternative for thalidomide **(12)**.

In a study, serum TNF-α was assayed before and during treatment with PTX in 15 patients with erythema nodosum leprosum (ENL). The increased TNF-α levels recorded in the circulation during the reaction were dramatically reduced within three to seven days of the initiation of therapy. In vitro TNF-α production was assayed upon mononuclear cell culture stimulation with Mycobacterium leprae. A reduction of inducible TNF-α in peripheral blood mononuclear cells was seen after one to two weeks of in vivo administration of PTX. These data suggest that PTX inhibits TNF-α production in ENL patients both in vivo and in vitro; thus it may be useful in the treatment of this type of leprosy reaction **(13).**

Various studies have documented that PTX rapidly ameliorates the systemic symptoms of type II leprosy reaction and it could be an alternative (though less effective) to thalidomide and a good option for patients with human immunodeficiency virus (HIV) co-infection, where steroids are contraindicated **(14).**

- **Acquired immunodeficiency syndrome and pruritic papular eruption of HIV/AIDS**

Increased levels of TNF-α have been demonstrated in many patients with AIDS. Pentoxifylline has been shown to decrease TNF-α expression, serum fasting triglycerides, and HIV replication in these patients. Also, it has been documented that PTX is a safe and efficacious treatment for the pruritic papular eruption of HIV/AIDS, a common and usually recalcitrant manifestation of HIV infection (15).

- **Leishmaniasis**

Pentoxifylline suppresses TNF-α gene transcription, potentiates the expression of inducible nitric oxide (NO) synthetase leading to NO production, and decreases leukocyte migration and adhesion .TNF-α seems to play a great role in the pathogenesis of mucosal leishmaniasis and PTX has been proposed for the treatment of cutaneous and mucocutaneous leishmaniasis as adjuvant to pentavalent antimony, which reduces the healing time

significantly and prevents the need for further courses of pentavalent antimony. The combined therapy with glucantime and PTX has been found to be more effective than glucantime alone **(16).**

Also, a previous study has shown that PTX can prevent renal functional alterations induced by meglumine antimonate in rats.Therefore, it seems that PTX is an ideal adjuvant in treating patients with leishmaniasis **(17)**.

- **Psoriasis**

The prototype of TNF-α-mediated diseases in dermatology is psoriasis. Indeed, some of the new biologic drugs for psoriasis act by inhibiting this cytokine. The beneficial effects of PTX in psoriasis have been shown in nude mice in both in vivo and in vitro studies, but there is a lack of sufficient studies in humans **(18).**

Pentoxifylline can be used also as an adjuvant therapy in psoriasis. It has been suggested that PTX counteracts many of the unwanted effects of cyclosporine on red blood cells, platelets, and coagulation factors. One study has shown that PTX ameliorates cyclosporine nephrotoxicity in humans. In addition, abnormal metabolism of triglyceride is not an uncommon finding in psoriatic patients and maybe also exaggerated after cyclosporine therapy. Because a possible benefit of PTX is in reducing serum triglycerides, it seems that a combination of PTX and cyclosporine is a very sensible choice. Randomized, clinical trials are needed to compare both the clinical response and lipid profiles in psoriatic patients on cyclosporine with or without adjuvant PTX **(19).**

Furthermore, there is also some evidence that concomitant PTX therapy may reduce the incidence and severity of gastrointestinal complaints and flushing in patients receiving fumaric acid esters, a widely used anti-psoriatic drug in northern Europe **(20).**

- **Graft-versus-host disease**

Cytotoxic T lymphocyte mediated tissue injury and inflammatory cytokines including TNF-α play important roles in the pathogenesis of GVHD. Using PTX in combination with other treatments could result in lower relapse rates and improved overall event free survival. However, the prophylactic role of PTX in GVHD is conflicting **(21).**

- **Sarcoidosis**

Although a specific inciting antigen for sarcoidosis has not yet been identified, it appears to be Th1 mediated disease and TNF-α likely plays a critical role in the granuloma formation. Pentoxifylline can almost completely inhibit spontaneous TNF-α production from alveolar macrophages of sarcoidosis patients; thus, a potential role in the treatment of pulmonary sarcoidosis, but there is little evidence as yet, about its role in cutaneous sarcoidosis **(22).**

- **Peyronie's disease**

Pentoxifylline is a non-specific phosphodieste inhibitor, which downregulates transforming TGF-β1, increases fibrinolytic activity, and increases NO levels, so the possible role of PTX to prevent progression of Peyronie's disease, reverse fibrosis, improve penile curvature and ultrasonographic appearance of the plaque and stabilize or reduce calcium content in penile plaques **(23)**.

- **Radiation induced fibrosis and burns**

Radiation induced fibrosis is mediated by TGF-β, besides its central role in scleroderma. Pentoxifylline reduces TGF-β induced collagen biosynthesis. In addition, fibroblast collagenases are also activated. Hence, the treatment of radiation-induced fibrosis with PTX and vitamin E can be a practicable and cost-effective regimen, especially for inoperable patients. Pentoxifylline has been found to have a direct effect on inhibiting burn scar fibroblasts and it can be potentially useful for reducing burn scar contractures in future **(24).**

- **Oral sub-mucous fibrosis**

Oral sub-mucous fibrosis is a common premalignant condition in the Indian subcontinent, caused by chewing areca nut and other irritants in various forms. The efficacy of PTX in oral sub mucous fibrosis, singly and as adjuvant therapy, has been demonstrated in various studies **(25).**

Pentoxifylline exerts its primary anti-fibrotic effects in oral submucous fibrosis (OSMF) through the non-selective inhibition of phosphodiesterase (PDE). This action prevents the degradation of cyclic adenosine monophosphate (cAMP), causing its continuous intracellular accumulation within mucosal fibroblasts. Elevated cAMP fundamentally disrupts pathological collagen homeostasis by directly suppressing fibroblast proliferation and downregulating the synthesis of extracellular matrix proteins. Furthermore, PTX actively promotes tissue remodeling by stimulating local collagenase and plasminogen activator activity, which actively facilitates the breakdown and resorption of the dense, pathological collagen bands deposited in the lamina propria **(26).**

Concurrently, PTX acts as a potent hemorheological modifier to reverse the severe tissue ischemia caused by the collagen-induced strangulation of local microvasculature. By increasing intracellular ATP and reducing calcium, it enhances erythrocyte deformability and lowers blood viscosity, which restores oxygen delivery to hypoxic tissues and halts the ischemia-induced fibrogenic loop. Additionally, PTX exhibits profound immunomodulatory properties by suppressing the transcription of Tumor Necrosis Factor-alpha (TNF-α) and interleukin-6 (IL-6). This effectively silences the upstream chronic inflammatory cascades responsible for persistent leukocyte recruitment and continuous fibroblast activation in the oral mucosa **(27).**

- **Pseudoxanthoma elasticum**

The use of PTX for ischemic pain in pseudoxanthoma elasticum and other micro vascular disorders has been encouraging **(28).**

In pseudoxanthoma elasticum (PXE), *ABCC6* mutations induce progressive mineralization of vascular elastic fibers, precipitating severe peripheral arterial disease and ischemia. Pentoxifylline mitigates these ischemic symptoms primarily through hemorheological modulation rather than reversing the genetic pathology. By inhibiting phosphodiesterase, PTX elevates intracellular cyclic adenosine monophosphate (cAMP), significantly enhancing erythrocyte deformability. This vital rheological adaptation allows red blood cells to physically navigate the rigid, calcified microvasculature typical of PXE, restoring critical tissue perfusion and alleviating intermittent claudication **(29)**.

Concurrently, PTX provides essential anti-thrombotic and anti-inflammatory benefits that further counteract vascular compromise in PXE. The agent decreases systemic blood viscosity and impedes localized platelet aggregation, substantially reducing the risk of thrombosis in stenotic arteries. Furthermore, PTX attenuates chronic endothelial inflammation by suppressing pro-inflammatory cytokines such as Tumor Necrosis Factor-alpha (TNF-α). Although highly effective for ischemic pain, PTX must be administered cautiously in PXE patients due to the condition's inherent predisposition to gastrointestinal hemorrhage **(30).**

- **Actinic prurigo**

Actinic prurigo (AP) is an immune-mediated photodermatosis driven by a delayed-type hypersensitivity to ultraviolet (UV) radiation and excessive Tumor Necrosis Factor-alpha (TNF-α) production. Pentoxifylline mitigates AP primarily through its immunomodulatory properties. By inhibiting phosphodiesterase and elevating intracellular cAMP, PTX directly suppresses TNF-α transcription and synthesis in immune cells. This targeted cytokine blockade effectively halts the primary inflammatory cascade responsible for the severe pruritic lesions **(31)**.

Additionally, PTX protects the epidermis from localized UV-induced cellular damage by significantly reducing the formation of apoptotic "sunburn cells". The agent concurrently inhibits the local activation and infiltration of T-lymphocytes and neutrophils in sun-exposed areas. Through these synergistic anti-apoptotic and anti-inflammatory mechanisms, PTX suppresses the abnormal local immune response, facilitating clinical remission and alleviating severe pruritus in AP patients **(32).**

- **Irritant and allergic hypersensitivity reactions**

Pentoxifylline mitigates both irritant and allergic contact hypersensitivity reactions primarily by inhibiting phosphodiesterase and elevating intracellular cAMP, which profoundly suppresses the production of Tumor Necrosis Factor-alpha (TNF-α) by leukocytes. Because TNF-α is the critical cytokine driving hapten-induced

inflammation, its targeted blockade effectively blunts the elicitation (effector) phase of delayed-type hypersensitivity. Consequently, pentoxifylline dampens local leukocyte activation and significantly reduces the inflammatory sequelae of both antigen-specific allergic contact dermatitis and non-specific irritant exposure **(33).**

- **Alopecia Areata (AA)**

Pentoxifylline is effective in the treatment of localized AA as well as triamcinoone acetonide injection. However, combined therapy with TAC is more effective than singly used injection **(34)**.

The response of intralesional TAC depends on several factors. The decreased expression of thioredoxin reductase 1 in the outer root sheath may be the cause for glucocorticoid resistance in some patients with AA, which is not needed for PTX action **(35).**

Pentoxifylline can prevent vasoconstriction and atrophy effects of TAC injection. The mechanism (s) by which PTX protects against vasoconstriction could be mediated by reduction in the associated low grade inflammation and oxidative stress, especially in cases of AA **(36).**

- **Lipodermatosclerosis**

Lipodermatosclerosis is a severe fibrosing condition driven by chronic venous hypertension and localized microvascular ischemia. Pentoxifylline mitigates this by inhibiting phosphodiesterase, thereby significantly increasing erythrocyte deformability and reducing overall blood viscosity. This hemorheological modification enhances microcirculatory blood flow through the congested venous beds, effectively restoring oxygen delivery to the ischemic subcutaneous tissues **(37).**

Concurrently, pentoxifylline exerts potent anti-inflammatory and anti-fibrotic effects critical for reversing the characteristic subcutaneous induration. Elevating intracellular cAMP suppresses the production of Tumor Necrosis Factor-alpha (TNF-α), thereby dampening chronic localized inflammation. Furthermore, it directly inhibits fibroblast biosynthesis of collagen while stimulating collagenase activity, actively reducing dermal fibrosis and promoting tissue repair **(38).**

- **Ulcerating necrobiosis lipoidica**

Ulcerating necrobiosis lipoidica is driven by severe microangiopathic ischemia, collagen degeneration, and granulomatous inflammation. Pentoxifylline promotes ulcer healing primarily through its hemorheological effects; by increasing erythrocyte deformability and decreasing blood viscosity, it restores vital microcirculatory perfusion to the ischemic dermal capillary beds. Concurrently, pentoxifylline inhibits phosphodiesterase to suppress tumor necrosis factor-alpha (TNF-α), effectively dampening the underlying granulomatous immune response and halting further structural collagen degradation **(39)**.

- **Kasabach-Merritt syndrome, pretibial myxedema**

Because of its anti-fibrinolytic effect, PTX could be useful in treating fibroblast-mediated diseases such as pretibial myxedema, resulting in reduction of thickness of skin lesions, when used in combination with topical or intralesional steroids **(40).**

- **Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)**

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe immune-mediated reactions characterized by widespread keratinocyte apoptosis. This massive cellular death is primarily driven by cytotoxic T-cells and the explosive release of pro-apoptotic cytokines, most notably Tumor Necrosis Factor-alpha (TNF-α) **(41)**.

Pentoxifylline mitigates SJS/TEN by inhibiting phosphodiesterase and elevating intracellular cAMP, which profoundly suppresses the systemic release of TNF-α. By neutralizing this critical pro-apoptotic cytokine, pentoxifylline halts the death-receptor signaling cascades that cause rapid epidermal detachment and tissue necrosis **(42)**.

- **Keloids, scleroderma and morphoea**

The effectiveness of PTX in the treatment of fibrosis via attenuating and reversing fibrotic lesions has been demonstrated in several clinical trials and animal studies. As a result, it is important to consider the potential clinical utility of PTX in the treatment of fibrosis **(4).**

Because of the inhibitory effects of PTX on the proliferation and certain biosynthetic activities of fibroblasts derived from human skin, it has a potential adjuvant role for keloids, hypertrophic scars, morphea, scleroderma, and other fibrosing conditions **(21)**.

Other uses

Pentoxifylline may also be beneficial in other diseases such as Kimura's disease with oral ulcers, generalized granuloma annulare, sweet syndrome, pemphigus vulgaris, and other bullous disorders **(43)**.

Non-Dermatological Uses

In addition to intermittent claudication, PTX has found application in varied disease processes; although, the mechanism is not fully elucidated in every case. The drug is gaining acceptance for conservative treatment of neuropathic injuries; prevention of thromboembolic strokes and septic shock; management of sickle cell disease; nausea and headaches in high altitude mountain sickness; acute alcoholic and non-alcoholic steatohepatitis and alcoholic liver disease, presumably through its ability to inhibit TNF; treatment of endometriosis, stimulation of various sperm motion parameters and cervical mucus penetrability in patients with asthenozoospermia, to mention just a few **(44).**

Checklist before prescribing PTX

While prescribing PTX, the following parameters should be specifically considered:

- Allergy to caffeine-containing products (coffee, tea, colas), PTX, theobromine, theophylline, or any other drugs
- Prior medications, especially anticoagulants (blood thinners) such as warfarin (Coumadin) and vitamins.
- Kidney disease.
- Pregnant, planning pregnancy or lactating.
- Any surgery in the near future.
- Advice to avoid driving a car or operating machinery **(2).**

Adverse effects of PTX:

Overall, PTX is a very safe drug and is usually well tolerated. The side effects are dose-related and the most common are those of the gastrointestinal tract and central nervous system. The main central nervous system side effects are dizziness, headache, anxiety, and confusion **(3).**

Contraindications of PTX

- Pregnancy: Pregnancy category C.
- Lactation: Pentoxifylline is excreted in breast milk and may cause adverse effects in the infant.
- Children: Safety and efficacy not established.
- Geriatric: Use with caution, usually starting at the lower dosage range, because of the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant diseases or other drug therapy.
- Other contraindications include previous hypersensitivity reactions to xanthine-related products, e.g. caffeine, theophylline, and theobromine; recent cerebral and/or retinal hemorrhage; porphyria **(2)**.

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