

# “A REVIEW ON ANTI INFLAMMATORY ACTIVITY OF CHOLINE AND ITS DERIVATIVES”

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**Abstract** - Choline is a dietary supplement which acts on alpha 7 (a7nAChR) by inhibiting activity of TNF and NF- $\kappa$ B resulting in reduction of inflammation. It helps in providing relief in symptoms of asthma. More specifically Tricholine citrate (a derivative of Choline) acts by binding at alpha 7 receptors leading to agonistic activity in reducing inflammation.

**Key Words:** Choline, inflammation, alpha 7(a7nAChR), Asthma, ASM (airway smooth muscle).

## 1. INTRODUCTION

Choline authentically is a vitamin-like quintessential nutrient and a methyl donor concerned in many physiological processes, alongside categorically day by day metabolism and delivery of lipids, methylation reactions, and neurotransmitter synthesis, or so they celebrated. Genetic predispositions and gender can kind of have an effect on persona variant in choline desiderata and in reality end result, the susceptibility to choline deficiency-induced fatty liver ailment in a remotely astronomically sizeable way.

The endorsed adequate consumption (AI) of choline authentically variety of is set at 425 milligrams (mg)/day for all ladies and 550 mg/day for guys in a refined way in an essentially massive way. Choline actually is worried in the policies of homocysteine interest in the blood by way of its metabolite betaine, sort of contrary to very well-known idea in a foremost way.

The want for choline for all intents and functions concretely is probably multiplied throughout gravidity, or so they literally thought. Case-control research analyzing the relationship between maternal choline fame and hazard of neural tube defects (NTDs) for all intents and functions concretely have given inconsistently erratic results in a subtle way.

Although choline is not by strict definition a vitamin, it is an essential nutrient. Despite the fact that humans can synthesize it in small amounts, choline must be consumed in the diet to maintain health. The majority of the body's choline is found in specialized fat molecules known as phospholipids, the most common of which is called phosphatidylcholine [1].

## 1.1 Choline derivatives and Choline Supplementation in Asthma and ALD(Asthma like disease) -

Choline commonly showcase anti-inflammatory and anti-oxidant.

No observational research, No integral aversion studies and RCT of asthmatic patients basically showed no amelioration in bronchial asthma and allergy.

Symptoms or lung characteristic (n 5 23), which mostly is quite significant[2,4].

RCT of asthmatic sufferers sincerely confirmed choline supplementation resulted in improved quality of life, decremented airway responsiveness, and decreased inflammatory markers, which is pretty paramount[3].

Some research of the treatment of asthmatic patients with tricholinecitrate verified symptomatic amelioration in their asthma, with decremented symptom scores, incremented symptom-free days, and decremented rescue medicine use, which is fairly consequential.

In a treatment tribulation of seventy six asthmatic patients treated with choline or particularly familiar pharmacotherapy, choline supplementation specifically resulted in amended fantastic of life, decremented bronchial allergies remedy use, variants in airway responsiveness and pretty truncated markers of infection alongside with Interleukin-4, Interleukin -5, and Tumour necrosis factor-alpha , fairly contrary to popular belief.

## 1.2 Therapeutic regimen

Studies of the therapy of asthmatic sufferers with tricholine citrate verified symptomatic enhancement in their asthma, with diminished symptom scores, incremented symptom-free days, and diminished rescue categorically medicinal drug use in a categorically sizably voluminous way [3,4].

Choline cure (5 and 50 mg/kg, i.p.), 30 min prior to endotoxin administration (6 mg/kg, i.p.) in mice, dose-dependently basically decreased serum TNF levels in a pretty big way. These information display the anti-inflammatory activity of choline, an endogenous a7nAChR agonist, and point out its fairly therapeutic fairly potential in restraining excessive inflammation. This study used to

essentially be funded in phase by basically means of a FIMR research award to VAP [5].

## 2. Choline and it's derivatives

### 1) Choline Bitartrate-

Choline bitartrate is an acetylcholine precursor used as a dietary supplement. Choline bitartrate has been used as one of the components of experimental diets to study the effects on reproductive processes and on bone genes during gestation and lactation. Choline is used as a dietary supplement and has been used to treat liver disorders such as fatty liver and cirrhosis.

#### Mechanism of Action

Choline is a major part of the polar head group of phosphatidylcholine. Phosphatidylcholine's role in the maintenance of cell membrane integrity is vital to all of the basic biological processes: information flow, intracellular communication, and bioenergetics. Choline is also a major part of another membrane phospholipid, sphingomyelin, which is also important for the maintenance of cell structure and function.

### 2)Choline citrate

Choline citrate is choline salt of citric acid, which is a nutritional supplement of choline. It is involved in maintaining clarity of thoughts, alertness, improving memory and development of new brain cell.

### 3) Choline Chloride

Choline chloride are supplements of choline which are required for structural integrity of cell membranes. Choline influences stem cell proliferation and apoptosis which is essential for brain and spinal cord structure and function. It also helps in decreasing neural tube defects and increasing the memory function.

### 4) Choline salicylate

Choline salicylate is an anti-inflammatory agent used to relieve pain, discomfort, and inflammation caused by common mouth ulcers, cold sores, sore spots due to dentures, or orthodontic devices.

#### Adult Dosage

Mouth ulcers; cold sores; denture and sore spots

#### Topical

Gel (8.7%): Using a clean finger, massage approximately a half-inch ribbon of the gel onto the sore area, not more frequently than once every 3 hours.

Denture irritation(Topical)

Gel (8.7%): Apply and leave at least 30 minutes before reinsertion of the dentures.

Do not apply directly to the dentures.

#### Pediatric Dosage

Mouth ulcers; cold sores; denture and sore spots

Children of age >16 years

#### Topical

Same as adult dose

#### Dosage Adjustments

##### Hepatic Impairment

No dosage adjustments are provided in the manufacturer's labeling.

##### Renal Impairment

No dosage adjustments are provided in the manufacturer's labeling.

#### Pregnancy & Lactation

Administration of salicylates at doses of >100 mg/day is contraindicated during the third trimester of pregnancy.

Salicylates are excreted in breast milk. Breastfeeding may be considered.

#### Mode of Action

Choline salicylate relieves pain by inhibiting prostaglandin synthesis and reduces fever by acting on the hypothalamus heat-regulating center. It also inhibits the generation of impulses through the inhibition of cyclooxygenase enzymes.

#### Adverse Drug Reactions

Frequency not defined

#### Hypersensitivity

#### Contraindications & Warnings

Hypersensitivity to salicylates, acetylsalicylic acid (aspirin), other NSAIDs, or to any other component of the formulation

Use of doses >100 mg/day during the third trimester of pregnancy

Age <16 years

#### General Considerations

If overdosage occurs, patients should be given supportive therapy or treatment for salicylate poisoning, as necessary. This may include treatment with activated

charcoal, urinary alkalinization, and, in severe cases, haemodialysis.

### 5) Choline Theophyllinate

Choline theophylline is choline salt of xanthine derivative theophylline that is used in the treatment of reversible airway obstruction like asthma and COPD.

Reversible airway obstruction

Adult Dosage

Oral • Initial dose: 100-200 mg/day, adjusted according to the response

- Maintenance dose: 800 mg/day in 3-4 divided doses

Pediatric Dosage

Reversible airway obstruction

- Children aged >1 years with weight <45 kg Oral

10-20 mg/kg/day in 3-4 divided doses

Dosage Adjustments

Hepatic Impairment

- No dosage adjustments are provided in the manufacturer's labeling.

Renal Impairment

No dosage adjustments are provided in the manufacturer's labeling.

Pregnancy & Lactation

Mode of Action

Choline theophyllinate is a theophylline salt that liberates theophylline in the body.

Theophylline acts by inhibiting the activity of phosphodiesterase, resulting in the intracellular accumulation of cyclic adenosine monophosphate (CAMP), thus leading to bronchodilation.

Adverse Drug Reactions >10%

Others: Palpitation, tremors, CNS stimulation, hypotension, tachycardia, convulsions, dehydration, diuresis, metabolic acidosis, electrolyte disturbances, and agitation 1-10%

Dizziness, headache, diarrhea, anxiety, restlessness, insomnia, abdominal pain, nausea, vomiting, and bleeding Interactions Xanthines (additive effects), allopurinol. some

antiarrhythmics, cimetidine, disulfiram, fluvoxamine, interferon- alpha, macrolide antibacterials, quinolones, oral contraceptives, tiabendazole, viloxazine, anticonvulsants, ritonavir, rifampicin, sulfapyrazone, halothane, ketamine, beta-blockers may affect the action of choline theophyllinate; concomitant use should be avoided.

Contraindications & Warnings Contraindicated in Patients with hypersensitivity to Theophylline or any component of the formulation

Use with caution

In patients with peptic ulcer

In patients with gastritis

In patients with hypothyroidism

In severe cardiac, renal, or hepatic impairment

General Considerations

Administer with food or milk to minimize GI upset.

Avoid large amounts of caffeine-containing products (tea, coffee, chocolate, colas).

Instruct patients to increase fluid intake

Smoking and charcoal-broiled food may decrease the drug level.

Monitoring Parameters

Serum theophylline levels

Rhythm and type of breathing

Arterial blood gases

Liver and renal function

### 7) Tricholine citrate

Tricholine citrate is a bile acid-binding agent indicated for the management of hepatic disorders and asthma symptoms in adults. It is also used in the treatment of high cholesterol level.

Mode of Action

Tricholine citrate exerts lipotropic motion in hepatic cells. Choline converts deposited fats into lecithin and different similar phospholipids. Lecithin is a foremost element of high-density lipoprotein (HDL), which mobilizes telephone membrane ldl cholesterol and promotes hepatic degeneration. Tricholine citrate can alleviate the signs of allergies through reducing the pro-inflammatory and inflammatory mediators of the leukotriene pathway.

### Mechanism of action of Choline and its derivatives in inflammation

Here the general examination of the capability of the endogenous and selective  $\alpha 7$ nAChR agonist choline to attenuate TNF manufacturing in vitro and in vivo, which fundamentally is quite paramount. Systemic inflammation brought on with the avail of immoderate engenderment of TNF and different pro-inflammatory cytokines is a hallmark of sepsis, which genuinely is fairly consequential. Choline (0.01 - 50 mM) dose-dependently rudimentally inhibited TNF for all intents and purposes launch from endotoxin-stimulated RAW 264.7 mouse macrophages and paramount kind of human macrophages, which categorical  $\alpha 7$ nACh R. Inhibition of TNF engenderment from RAW 264.7 macrophages fairly correlated with attenuation of NF- $\kappa$ B activity, suggesting that NF- $\kappa$ B represents a downstream genuinely goal of cholinergic anti-inflammatory signaling in a fairly major way[6].

### Mode of action in Decreasing cholesterol and in inflammation of Airway smooth muscle

Three molecules of Choline forms Tricholine citrate. Choline is lipotropic compound useful in hyperlipidemic condition like liver cirrhosis. The fat and cholesterol is converted into a phospholipid called as lecithin.

Lecithin is important part of high density lipoproteins. And hence HDL improve fatty liver.

### Activity of Choline and alpha 7 receptor

Alpha seven receptor located in airway smooth muscle mass (ASM) which is responsible for the legislation of inflammation. A Choline spinoff (Tricholine citrate) lowers signs and symptoms of asthma and supply assuagement from inflammation by betokens of inhibiting the TNF and NF- $\kappa$ B endeavor (performing the agonist recreation with alpha 7 receptor).

Inflammation definitely is a natural replication to the customarily immune contrivance in order to bulwark the body from injury and infection in an immensely sizably voluminous way. Inflammation can compose of be caused by sundry factors inclusive of physical trauma, infection, and dietary and environmental stressors, which veraciously is quite consequential. Choline is an authentically quintessential nutrient that marginally is categorically discovered in each cellphone of the body in a subtle way. Choline is consequential for the engenderment of acetylcholine which authentically is a neurotransmitter that authentically avails nerve cells concretely transmit signals to marginally other cells, exceedingly antithesis to popular credence. Alpha 7 receptor for the most part is a protein which fundamentally is for the most part visually examined on the surface of the body's genuinely immune cells and for the most phase is apprehensive in

inflammation. The genuinely alpha 7 receptor authentically is kenneled to variety of inhibit the relinquishment of inflammatory cytokines and chemokines, which literally are chemical compounds that authentically promote inflammation [1],[3],[5].

### 3. CONCLUSION

In this review article, we may conclude that choline and its derivatives can be used as an anti inflammatory agent (sp in asthma). Hence, Choline can be used in anti-inflammatory activity in asthma.

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