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# A Review: Neurological effects of camphor

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**ABSTRACT:** Aromatic and volatile terpene ketone camphor is extracted from Cinnamonumcamphora wood or manufactured from turpentine. The effects of camphor, a stimulant of central nervous system, may vary from little excitement of CNS to full-blown convulsions. Camphor readily enters the brain because of its high lipid solubility. It's a neurotoxic substance, therefore avoid it at all costs. The neurological signs of dependence & withdrawal from camphor are widespread in India. Even in small amounts, camphor is hepatotoxic. The purpose of this paper is to offer a synopsis of camphor's pharmacological and toxicological properties so that safety & risk associated with its usage may be assessed.

**Keywords:** Camphor, Neurotoxic, Antidepressant, Anticonvulsant, Antioxidant, Anti Alzheimer.

## I. INTRODUCTION

Natural camphor is extracted from at least 50-year-old camphor laurel trees using steam distillation and sublimination. You can also get it from herb Lippia dulcis Trev., although it's not used commercially, and it's found in a few other laurel family trees including Ocoteausambarensis Eng. Camphor is mostly sourced from the Ocimumkilimandscharicum Baker ex Gurke[1] tree in Asia. Dehydronorbornyl chloride is an intermediate in the synthetic production of camphor using vinyl chloride & cyclopentadiene. Natural forms are dextrorotatory, whereas their synthetic counterparts are optically inactive. Camphor is widely used in liniments for the treatment of fibrositis, neuralgia, and related illnesses because of its anti-inflammatory, antibacterial, & antimicrobial characteristics & its rubefacient and moderate analgesic effects. Camphor contains modest expectorant qualities and irritating and carminative characteristics if consumed. It is risky to use camphorated-oil, suspension in oil administered intramuscularly or subcutaneously, like a respiratory and circulatory stimulant. In the past, it's utilised to help disperse bile duct stones alongside menthol & chenodeoxycholic acid, however it's no longer advised. [2,3].

### Pharmacology

### Pharmacodynamics

Camphor, product of Cinnamomum camphora tree, has been used medicinally for centuries[4] as an antibacterial, analgesic, antipruritic, counterirritant, & rubefacient. The mild local anesthetizing effect & developing of circumscribed sensory experience of heat, as well as the distinctive & penetration of odor that is mostly people associated with impression of a powerful & effectual medicine, contribute to its prevalent medicinal usage, predominantly into topical provisions. [5].

Camphorated oil, preparation having 19% to 20% camphor together in carrier oil, is popular type of camphor used today, both as an inhalant & like primary active component in liniments & balms utilized for topical analgesics[6].

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Camphor and its derivatives were among of first drugs to have their effects upon coughing, nasal congestion, & coughing fits rigorously studied.

It seems that the activation of cold receptor with in nose contributes to its nasal decongesting function, rather than just being a mechanical effect. Camphor (also eucalyptus &menthol) vapor inhalation upon group of volunteers enhanced feeling of airflow in nose by inducing a chilly sensation into nose, but having no effect on nasal impedance for airflow [7].

Newer research has linked camphor's effects on bronchospasm towards its anti-histaminergic as well as anti-cholinergic actions, and its antispasmodic impact to its effectiveness in treating the common cold. In fact, camphor seems to be beneficial in decreasing bronchoconstriction induced by histamine H1 & muscarinic M3 receptors, so this activity is related to suppression of coughing as well [8].

Animals subjected to a chemically induced cough were given inhalations of camphor aromatic vapor at doses of 50, 133, & 500 µg l-1[9]. The lowest doses had no impact, but at 500 g l-1, camphor decreased cough intensity by 33% and increased cough latency by same amount[10,11].

Even though camphor's analgesic properties are well recognized and used, little is understood about the chemical processes that underpin them[12].

Camphor causes stimulation and desensitization of sensory neurons by activating TRPV3,[13] a member of the transient receptor channel superfamily, as shown by Moqrich et al. Applying camphor topically has the well-known effect of creating a feeling of health. In reality, TRPV3 is warmsensitive $Ca^{2+}$-permeable cation channels that, when activated, is responsible for the onset of the warm feeling by effectively imitating an elevation in local tissue temperature. Other natural chemicals, such as carvacrol, eugenol, & thymol, also have this effect, which is mediated from an upsurge on intracellular $Ca^{2+}$ levels.

Despite its analgesic properties, camphor may sensitize TRPV3 if used in large enough doses or over long enough periods of time.

In contrast, camphor's antipruritic and counterirritant activity is linked to its ability to activate TRPV1, another member of the TRP channel superfamily, so at level of dorsal root gangliar [DRG] neurons & block TRPA1 channels, action shared by other TRPV1 agonists[14]. Camphor's newly elucidated action as a TRPA1 inhibitor is used to pretreat human embryonic kidney cells before testing them for membrane possible changes triggered by thymol, demonstrating that camphor inhibits the response to thymol. experimental evidence in mice, using intradermal injection of acetaldehyde into the mouse footpads, shown that camphor may reduce acute pain[15,16]. In the field of radiotherapy, camphor has the potential to serve as a radiosensitizing agent. Male C3H/Jax mice with transplanted mammary tumors were given camphor (0.5 mol á body wt-1) 45 mins prior receiving local x-irradiation at 30, 80, 100, or 120 Gy. Optimal augmentation proportions in tumor growth were found to be delayed by 4.8 days when tumor volumes were measured sequentially for 45 days following radiation treatment. [17].

**Pharmacokinetics**

Inhalation, ingestion, and skin contact all result in rapid absorption of camphor[18]. When 200 mg of camphor was consumed without any kind of solvent, maximum plasma levels were achieved 3 hours later.

When applied topically, skin absorption is quick but rather little in volume. Camphor levels in the plasma were measured by selective gas-chromatography after human participants had patches of varying strengths (2, 4, or 8) applied to their skin for 8 hours. Camphor plasma concentrations peaked at 35.2 to 46.8 ng/ml-1 when 8 patches were applied, 19.6 to 34 ng/ml-1 when just 4 patches were used, and were almost undetectable when only 2 patches were used, demonstrating rapid but not huge dermal absorption.

Because camphor travels throughout the body and crosses the placenta, it is not advised that it be used during pregnancy or during nursing [19].

It is estimated that 61% of the drug is bound to proteins in the plasma. The distribution volume is 2 to 4 L/kg[20].

Camphor is metabolized into hydroxycamphor metabolites in the liver after absorption, distribution, and elimination.

from the urine of camphor-fed dogs, I isolated cis- and trans-$^{1}$-hydroxycamphor and camphor-1-carboxylic acid; from the urine of rabbits, I isolated 5-hydroxycamphor [as major metabolite] and 3-hydroxycamphor; and from the urine of dogs, I obtained 15% 3-hydroxycamphor, 55% 5-hydroxycamphor, and 20% trans-1-hydroxycamphor, as reported by Shimamoto (1934).

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Both (+)-camphor and (-)-camphor were shown to increase the concentration of glucuronide in rabbit urine by Robertson and Hussain (1969); (+)-camphor was also hydroxylated to (+)-5-endohydroxycamphor & (+)-3-endo-hydroxycamphor[21], while (+)-borneol was reduced to (+)-camphor.

To a large extent, cytochrome P450, a family of heme-containing monooxygenases found throughout the body, is responsible for the hydroxylation of camphor, norcamphor, pericyclocamphanone, and 5,5-dißuorocamphor[22]. Non-enzymatic hydroxylation of camphor mostly yields 3-hydroxycamphor, whereas cytochrome P450 is responsible for the conversion of camphor to 5-hydroxycamphor (Gelb et al., 1982)[23]. The hydroxylation of camphor and similar compounds by cytochrome P450 happens with distinct area specificities. [24].

Metabolite hydroxylation is followed by glucuronic acid conjugation and subsequent urinary excretion. Two hundred milligrams of camphor has a 167-minute half-life when taken orally on its own, but just 93 minutes when taken with a solvent.

The enzymes in the liver responsible for metabolizing drugs in phases I and II may be affected by camphor. Female Swiss Albino mice were given 50, 150, or 300 mg/Kg-$^{1}$ of camphor dissolved in 0.1ml of olive oil once a day for 20 days. Camphor: the advantages and disadvantages it presents increased liver decreased glutathione levels through aryl-hydrocarbon hydroxylase & glutathione S-transferase[25].

**Interactionof Camphorwithothercompounds**

A synergic activity of the two preparations revealed in ameliorating cardiac performances, however there have been very few investigations of pharmacological interaction between camphor as well as other chemicals extract from fresh crataegus berries. While D-camphor seemed to be the key element in causing quick initial impact, extract added a long-lasting effect by increasing total peripheral resistance, which was caused by an increase in tone of arterioles. [26].

**Neurological Effectsof Camphor**

Depending upon that dosage & mode of administration, each pharmacological substance has both advantages and risks. When it comes to the nervous system, camphor has dual roles as both neuroprotective and neurotoxic.

**Neurotoxic**

Because of its ability to draw oil, the neurotoxic chemical camphor is readily absorbed by the mucosa, gastrointestinal tract, skin, and respiratory system[27]. Symptoms associated to the central nervous system, such as hyperactivity, tremor, headache, hallucinations, disorientation, delirium, clouded consciousness, and coma, may appear later, depending on the quantity consumed. Transaminase elevation, liver damage, hepatosteatosis[28], albuminuria, urine retention, and sinus tachycardia are other possible side effects. Asphyxiation results from respiratory stoppage and uncontrollable convulsions. If no adverse effects are seen within four hours of intake, research suggests that no further consequences will occur [29].

**Neuroprotective**

The camphor laurel, Cinnamomum camphora (C. camphora), and Artemisia fukudo both provide wood that contains camphor, a terpenoid. Positive benefits on antioxidants, inflammation, and cancer prevention were observed. Camphor is essential for proper immune system function and the inactivation of carcinogenic enzymes. It was also used to treat autism, Alzheimer's, memory difficulties, and other neurological conditions. The depressive symptoms of rats were alleviated by an increase in brain-derived neurotrophic factors & serotonin levels, which were shown to be increased by a camphor-containing hydroalcoholic extract of Cinnamomum.

Antidepressant Action[30]

Camphor's antidepressant benefits seemed to stem from its anti-inflammatory and antioxidant properties, which boosted catalase and Nrf-2 expression while reducing NO, MDA, TNF-a, & TLR4 synthesis. It may be useful for lowering ciprofloxacin-induced depression since it up-regulated P190-RHO GTP protein, which enhanced locomotor activities, & ameliorated neurotransmitters & histopathological alteration.

AnticonvulsantAction[31]

The increased GABA level, suppression of AChE and inflammation, & antioxidant activity in brain have all been linked to camphor as well as its extracts, suggesting they may have anticonvulsant & neuroprotective effects.

Antioxidant Action[32]

Camphor leaf organic crude extracts of varying polarities were produced by Muhamad et al. in 2019. Ethanol, hexane, and chloroform are

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among examples. According to the quantitative study, all extracts have high levels of antioxidant activity. The antioxidant activity of ethanol extracts was the greatest compared to other extracts. These results demonstrate that high antioxidant content of camphor leaves is useful in formulation of medicines, particularly those used to treat wounds.

Anti-Alzheimer Activity[33]

Multiple patents mentioned camphor's potential in treating neurological disorders. The use of camphor in the treatment and prevention of neurological disorders like Alzheimer's has been around for quite some time. Preparing and injecting a Cinnamomum camphora extract into an animal model of Alzheimer's-related dementia improved animal model's instantaneous spatial perception and mitigated decline in memory and learning confirming that concentrate might be efficaciously were using throughout relieving as well as classifying Alzheimer's-related dementia.

**Animal Modelsusedin Neurological Disorder**

Animal models are essential for the identification of novel treatments for neurological illnesses because they may be used to test potential treatments in advance of human clinical trials. The difficulty is in creating models that accurately represent the problem in both circumstances. Creating a model calls for input from many different fields of study. A framework of scientific criteria that a model must fulfill should be established by preclinical and clinical specialists. The scientific assessment takes into account the model's reproducibility, reliability, predictability, construct validity, external validity, generalizability, and relevance.

For gainingin depth& make forecastsregarding brain-behavior relations in humans and/or in species that was not researched, or in a similar species under circumstances distinct out of those in which research has been conducted, a biologically and/or clinically relevant animal model is used in the behavioral neurosciences.

Purposeof Animal Models

- ✓ to deepen our knowledge of the brain-behavior connection, or the fundamental substrates and processes that regulate typical and aberrant human behavior.
- ✓ to apply these findings from an animal investigation to human medicine.
- ✓ discovering novel pharmacological targets, routes, and modes of action
- ✓ evaluating the efficacy and potential side effects (teratology, toxicology, and safety) of substances or therapies thought to have neuroprotective, anti-degenerative, revalidation-supporting, mental health-promoting, or cognitive-enhancing properties.

Mice and rats are the go-to species for neuroscience studies because their brain complexity is strikingly comparable to that of humans, providing a useful window into the workings of the human brain. Genetic modification of mice is also feasible, allowing scientists to examine role of certain genes in disease development. Models of neurological diseases in animals.

- **MCAo**
- **Mouse MCAo**
- **Distal MCAo**
- **Embolic MCAo**
- **Photothrombosis model**
- **6-hydroxydopamine**
- **Rotenone**
- **Paraquat**

## II. CONCLUSION:

We have examined the use of camphor throughout history; it has been effectively utilized for years to treat skin conditions. Camphor has medicinal promise when used topically, but it also has neurotoxic potential, according to our review. We have discovered that camphor can have some positive effects when converted to its derivative form. There hasn't been much research done on camphor and its derivatives, though.

## REFERENCES

[1]. Compadre CM, Robbins EF, Kinghorn AD (1986) The intensely sweet herb, Lippia dulcis Trev.: historical uses, Field enquiries, and constituents. J Ethnopharmacol 15(1):89-106.
[2]. Budavari S (Ed.), (1989) The Merck Index. 11th Edition. Merck and Co Inc, Rahway, USA.
[3]. Reynolds JEF (Ed.), (1989) Martindale The Extra Pharmacopeia. 29th edition. The Pharmaceutical Press, London.
[4]. Hercogova J (2005) Topical anti-itch therapy. Dermatol Ther 18:341-343.
[5]. Lyne CB, Kraft JN, Lynde CW (2008) Novel agents for intractable itch. Skin Therapy Letters 13(1):6-9.
[6]. Gibson DE, Moore GP, Pfaff JA (1989) Camphor ingestion. Am J

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EmergCamphor: its benefits and risksMed 7:41-43.

[7]. Xu H, Blair NT, Clapham DE (2005) Camphor activates and strongly desensitizes the transientreceptor potential vanilloid subtype 1 channel in a vanilloid-independent mechanism. J Neurosci 25(39):8924-8937.

[8]. Burrow A, Eccles R, Jones AS (1983) The effects of camphor, eucalyptus and menthol vapour on nasal resistance to airßow and nasal sensation. Acta Otolaryngologica 96(1-2):157-161.

[9]. Astudillo A, Hong E, Bye R, Navaretta A (2004) Antispasmodic activity of Acalypha phleoides Cav. Phytother Res 18:102-106.

[10]. Gornemann T, Nayal R, Peretz HH, Melzig MF (2008) Antispasmodic activity of essential oil from Lippia dulcis Trev. J Ethnopharmacol 117:166-169.

[11]. Kreutner W, Hey JA, Anthes J, Barnett A, Young S, Tozzi A (2000) Preclinical pharmacology of desloratadine, a selective and nonsedating histamine H1 receptor antagonist. Arzneimittelforschung 50:345-352.

[12]. Lade EA, Morice AH, Grattan TJ (1994) The antitussive effects of menthol, camphor and cineole in conscious guinea-pigs. PulmPharmacol 7(3):

[13]. Moqrich A, Hwang SW, Earley TJ, Petrus MJ, Murray AN, Spencer KS, Andahazy M, Story GM, Patapoutian A (2005) Impaired thermosensation in mice lacking TRPV3, a heat and camphor sensor in the skin.

[14]. Nagata K, Duggan A, Kumar G, Garcia-Anoveros J (2005) Nociceptor and hair cell transducer properties of TRPA1, a channel for pain and hearing. J Neurosci 25(16):4052-4061.

[15]. Peier AM, Reeve AJ, Andersson DA, Moqrich A, Earley TJ, Hergarden AC, Story GM, Colley S, Hogenesch JB, McIntyre P, Bevan S, Patapoutian A (2002) A heat-sensitive TRP channel expressed in keratinocytes. Science 296:2046-2049.

[16]. Jordt SE, Julius D (2002) Molecular basis for species-speciÞc sensitivity to ÒhotÓ chili peppers. Cell 108(3):421-430.

[17]. Guilland-Cumming DF, Smith GJ (1982) The effect of camphor on mitochondrial respiration. Experientia 38(2):236-237.

[18]. Baselt RC, Cravey RH (1990) Disposition of toxic drugs and chemicals and drugs 3rd ed. Year Book Medical Publishers Inc.

[19]. Sweetman SC (ed.), (2005) Martindale: The Complete Drug Reference. 34th edition. The Pharmaceutical Press, London.

[20]. Koppel C, Tenczer J, Schirop T, Ibe K (1982) Camphor poisoning - abuse of camphor as a stimulant. Arch Toxicol 51:101-106.

[21]. Robertson JS, Hussain M (1969) Metabolism of camphors and related compounds. Biochemical Journal 113(1):57-65.

[22]. Wand MD, Thompson JA (1986) Cytochrome P450-catalyzed rearrangement of a peroxyquinol derived from butylated hydroxytoluene. Involvement of radical and cationic intermediates. J Biol Chem 261:14049-14056.

[23]. Land EJ, Swallow AJ (1979) Some free radical reactions of camphor in relation to the action of cytochrome P450. Journal of the Chemical Society, Faraday Transactions I 75:1849-1856.

[24]. Collins JR, Loew GH (1988) Theoretical study of the product speciÞcity in the hydroxylation of camphor, norcamphor, 5,5-dißuorocamphor, and pericyclocamphanone by cytochrome P450cam. J Biol Chem 263(7):3164-3170.

[25]. Banerjee S, Welsch CW, Rao AR (1995) Modulatory inßuence of camphor on the activities of hepatic carcinogen metabolizing enzymes and the levels of hepatic and extrahepatic reduced glutathione in mice. Cancer Letters 88(2):163-169.

[26]. Belz GG, Loew D (2003) Dose-response related efficacy in orthostatic hypotension of a Fixed combination of D-camphor and an extract from fresh crataegus berries and the contribution of the single components. Phytomedicine 4:61-67.

[27]. Manoguerra AS, Erdman AR, Wax PM, et al. Camphor poisoning: an evidence-based practice guideline for outof-hospital management. Clin Toxicol (Phila) 2006;44:357–70.

[28]. Camphor revisited: focus on toxicity. Committee on Drugs. American Academy of Pediatrics. Pediatrics. 1994;94:127–8.

[29]. Tekin HG. 2015 Seizures due to high dose camphor ingestion. Turk pediatriarsivi. 50(4): 248-250.
[30]. Salama A, 2022. Neuroprotective role of camphor ciprofloxacin induced depression in rats: modulation of Nrf-2 and TLR4. 309-312.
[31]. Jawaid T. 2018. Anticonvulsant and neuroprotective effects of methanolic extract of Cinnamomum camphora leaves in rat brain. Oriental pharmacy and experimental medicines.
[32]. Muhamad SHA. 2019. Antioxidant activity of camphor leaves extract based on variation solvent. Journal of physics. 1349.
[33]. PCT/KR2016/009447 2016 Pharmaceutical composition containing cinnamomumcamphora extract as active ingredient for the prevention and treatment of neurological diseases..