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Review on Medicinal Usefulness of Vitex negundo Linn

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Abstract

Vitex negundo Linn. is a woody plant found mainly in Indian subcontinent and its neighbouring countries. Almost all the sections of the plant possess a massive amount of phytochemical secondary metabolites that impart an unparalleled variety of medicinal uses of the plant. Point to note that a single plant species finds use for treatment of a large spectrum of human health ailments in traditional as well as folk medicines, lion part of which have been experimentally proved to be absolutely true. In fact the plant is a constituent of a number of commercially available herbal formulations and has also shown an efficient bio-control instrument. Exercise of biotechnologically advanced procedures would provide resources of rapid proliferation and management of the plant species and from the point of view of phytochemistry, it furnishes opportunities for augmentation of the quality and quantity of the biologically potent secondary metabolites occurring in the plant. In this paper the already reported medicinal uses and pharmacological activities of different parts of the plant have been reviewed.

Keywords

Vitex negundo, Medicinal Uses, Analgesic, Anti-Inflammatory, Antioxidant, Antifungal

1. Introduction

Our globe is slowly progressing towards herbal formulations which in practice are known to be extremely valuable against a large inventory of diseases and sicknesses. Moreover, they are not known to be responsible for any notable bad effects [1] and are readily available at inexpensive prices [2]. Prajapati *et al.* [3], however, cautioned us stating that plant medicines are efficient and without side-effects, provided that they are chosen prop-

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erly and taken under correct medical direction. The active constituent, habitually a secondary metabolite, differs in quality and quantity for a given plant species growing in different places. The market value of such plants depends on their active substance rather than simply on their ample growth. Purohit and Vyas [4] guess that roughly 70,000 species of the plant kingdom have been used as herbal medicine at one time or other.

Ethnobotany is considered as the study of the native uses of plants and the relationship between man and plants. Study of ethnobotany reveals that *Vitex negundo* has been used since ancient times as a female remedy [5]. It was found to diminish sexual desire and it is recorded that Roman wives whose husbands were abroad with the legions spread the leaves of *Vitex negundo* on their beds for this purpose [5]. Later, it became known as the chaste (meaning innocent or faithful) berry tree! During the middle ages, chaste berry is thought to effect on sexual desire that gradually made it a food spice at monasteries, where it was commonly called "Monk's pepper" or "Cloister" (a covered arcade usually meant for the monks) pepper [5]. In folklore, it was also acknowledged as an important European remedy for controlling and regulating the female reproductive system [5]. Long before, it was used as a regulator to menstrual periods and to treat amenorrhea (abnormal suppression of menstruation) and dysmenorrhea (painful menstruation). It also helped ease menopausal troubles and relieve the child birth process [5].

2. Plant Description

Vitex negundo is an erect shrub or a small tree that grows from 2 to 8 m in height. The bark is usually reddishbrown. Its leaves are branched into three to five finger like lanceolate leaflets (**Figure 1**). Each leaflet is around 4 to 10 cm in length, with the central leaflet being the longest and possess a stalk. The leaf edges are toothed or notched like saw and the bottom surface is covered with hair [6]. The copious purple-white flowers are borne in panicles about 10 to 20 cm in length (**Figure 1**). The petals are of different lengths, with the middle lower lobe being the longest. Both the corolla and calyx are covered in dense hairs [6]. The fragrant flowers are hermaphrodite [5] (have both male and female organs) in nature and are pollinated by insects.

Taxonomical classification: Kingdom—Plantae, Subkingdom—Tracheobionta, Superdivision—Spermatophyta, Class—Magnoliopsida, Subclass—Asteridae, Order—Lamiales, Family—Verbenaceae, Genus—*Vitex*, Species—*negundo*.

3. Distribution and Habitate

Vitex negundo is native to tropical Eastern and Southern Africa and Asia [7]. Countries it is indigenous to include Afghanistan, Bangladesh, Bhutan, Cambodia, China, India, Indonesia, Japan, Kenya, Madagascar, Malaysia, Mozambique, Myanmar, Nepal, Pakistan, the Philippines, Sri Lanka, Taiwan, Tanzania, Thailand, and Vietnam [7]. It is commonly found throughout India, mainly in warmer areas and ascending to an altitude of 1500 m in outer Western Himalayas [5]. The plant prefers sandy and loamy soils of acidic, neutral or basic character and requires well-drained soil. It can even grow in nutritionally poor soil [5]. The plant is generally found near water bodies, grasslands and mixed open forests [8].



Figure 1. The plant Vitex negundo with five lanceolate leaflets and panicles of purple-white flowers.

4. Phytochemistry

According to Namdeo [9], about a quarter of all the prescribed pharmaceuticals in developed countries include compounds that are directly or indirectly, obtainable from plants. *Vitex negundo* has been found to be a warehouse of a number of biologically active components or phytochemicals that possess generous use in the pharmaceutical industries. Generally, phytochemicals or secondary metabolites occur in the form of complex mixtures that differ among plant organs and stages of development [10] [11]. **Table 1** offers a detailed report of the different phytochemical constituents that have been isolated from different parts of *Vitex negundo*.

5. Medicinal Importance

The value of natural products in modern medicine has been well recognized. Inspection of medical indications by source of compounds has demonstrated that natural products and related drugs are used to treat about 87% of all categorized human ailments [27]. A report of World Health Organization says that more than 80% of world population depend on traditional medicine for their primary health care needs [28]. The increased interest in

Table 1. Phytochemical constituents of different plant parts of Vitex negundo.

Plant body part	Phytochemical components	References		
	5-hydroxy-3,6,7,3',4'-pentamethoxyflavone			
	6'-p-hydroxybenzoyl mussaenosidic acid; 2'-p-hydroxybenzoyl mussaenosidic acid			
	5, 3'-dihydroxy-7,8,4'-trimethoxyflavanone; 5,3'-dihydroxy-6,7,4'-trimethoxyflavanone			
Leaves	Viridiflorol; β -caryophyllene; sabinene; 4-terpineol; gamma-terpinene; caryophyllene oxide; 1-oceten-3-ol; globulol			
	Betulinic acid [3 β -hydroxylup-20-(29)-en-28-oic acid]; ursolic acid [2 β -hydroxylurs-12-en-28-oic acid]; n -hentriacontanol; β -sitosterol; p-hydroxybenzoic acid			
	Protocatechuic acid; oleanolic acid; flavonoids	[17]		
	Angusid; casticin; vitamin-C; nishindine; gluco-nonitol; p-hydroxybenzoic acid; sitosterol	[18]		
	3β -acetoxyolean-12-en-27-oic acid; 2α , 3α -dihydroxyoleana-5,12-dien-28-oic acid; 2β , 3α diacetoxyoleana-5,12-dien-28-oic acid; 2α , 3β -diacetoxy-18-hydroxyoleana-5,12-dien-28-oic acid			
Seeds	Vitedoin-A; vitedoin-B; α -phenylnaphthalene-type lignan alkaloid, vitedoamine-A; five other lignan derivatives			
	6-hydroxy-4-(4-hydroxy-3-methoxy-phenyl)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde	[22]		
	β -sitosterol; p-hydroxybenzoic acid; 5-oxyisophthalic acid; n -tritriacontane, n -hentriacontane; n -pentatriacontane; n -nonacosane	[18]		
	2β , 3α -diacetoxyoleana-5,12-dien-28-oic acid; 2α , 3α -dihydroxyoleana-5,12-dien-28-oic acid; 2α , 3β -diacetoxy-18-hydroxyoleana-5,12-dien-28-oic acid; vitexin and isovitexin			
Root	Negundin-A; negundin-B; (+)-diasyringaresinol; (+)-lyoniresinol; vitrofolal-E and vitrofolal-F			
	Acetyl oleanolic acid; sitosterol; 3-formyl-4,5-dimethyl-8-oxo-5H-6,7-dihydronaphtho- $(2,3\beta)$ -furan	[25]		
Essential oil of fresh leaves, flowers and dried fruits	δ -guaiene; guaia-3,7-dienecaryophyllene epoxide; ethyl-hexadecenoate; α -selinene; germacren-4-ol; caryophyllene epoxide; (E)-nerolidol; β -selinene; α -cedrene; germacrene D; hexadecanoic acid; p-cymene and valencene	[26]		

plant derived drugs is mainly because of the wide spread belief that the herbal medicines are safer than precious synthetic (mainly allopathic) drugs which, in general, possess side effects. On the other hand, there is a continuous development of resistant strains that pose the need for search and advancement of new drugs to cure diseases [29]. Usually, herbal medicines, rather than merely curing a particular disease, aims at returning the body back to its natural state of health [30]. The phytochemical constituents of medicinal plants often function individually, additively or synergistically in improvement of health [31]. After having analyzed the various chemical components available in different parts of *Vitex negundo*, it is essential that focus shifts to the medicinal applications of the plant. Many medicinal properties have been endorsed to *Vitex negundo* and the plant has also been comprehensively used in treatment of a large number of ailments [32]. These properties have been categorized under three heads—traditional medicine, folk medicine and pharmacological studies.

Traditional Medicine: Traditional medicine mainly comprises of Indian Ayurveda, Siddha, Arabic Unani and Chinese herbal medications. Largely in Asia and Latin America, people continue to use traditional medicine as a result of long past ritual and cultural beliefs. Traditional medicine accounts for a large part of all health care delivered in China. Even greater part of people in Africa depend on traditional medicines to help meet their health care requirements [33]-[36].

Ayurveda—*Vitex negundo* is mentioned in the verses of the *Charaka Samhita* which is unquestionably the most ancient and authoritative textbook of Indian *Ayurveda*. The plant has been designated as an anthelminthic (drugs that expel parasitic worms *i.e.*, helminths, from the body) (verse *Su*: 4 - 15) and is prescribed as a vermifuge (verse *Vi*: 7 - 21) in the description on the *Charaka Samhita* by Sharma [37]. Other Ayurvedic uses of *Vitex negundo* are illustrated by Tirtha [38]. People sleep on pillows stuffed with *Vitex negundo* leaves to get rid of catarrh (secretion of excess mucus through nose and throat because of cold) and headache and smoke the leaves for relief. Crushed leaf poultice is applied to cure headaches, neck gland sores, tubercular neck swellings and sinusitis. Essential oil of the leaves is also successful in treatment of sexually transmitted diseases and other syphilitic skin ailments. A leaf decoction with *Piper nigrum* is used in catarrhal fever with heaviness of head and dull hearing. Application of *Vitex negundo* for the treatment of dysmenorrhea in Ayurveda is reported by Jadav and Bhutani [39]. Patkar [40] noted to the preparations enumerated in *Anubhoga Vaidya Bhaga*, a compendium of formulations in cosmetology, in outlining the use of *Vitex negundo* leaves along with those of *Azadirachta indica, Eclipta alba, Sphaeranthus indicus* and *Carum copticum* in a prominent renovation treatment known as *Kayakalpa. Vishagarva taila*, an important Ayurvedic nervine sedative contains extracts of different parts of *Vitex negundo* [41].

Siddha—Reported to have evolved more than ten thousand years ago in southern India, the Siddha system of medicine is considered one of the most ancient traditional medical systems. The premier scientists of this system are known as Siddhars and Agathiyar is said to be the guru of all Siddhars whose numerous disciples wrote thousands of texts on Siddha, including medicine and formed the propounders of the system to the world. The Central Council for Research in Ayurveda and Siddha (CCRAS, New Delhi), established in 1978, by Department of AYUSH (Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy), Ministry of Health and Family Welfare, Govt. of India, coordinates and promotes research in this field. Also, the Central Council of Indian Medicine (CCIM, New Delhi), a statutory body established in 1971 under AYUSH, monitors higher education in the areas of Indian medicine, including Siddha.

Unani—Khare [42] outlines the purposes of *Vitex negundo*, commonly known as *Nishinda* in Unani medicine. The seeds are taken internally with sugarcane vinegar for elimination of bulges. Pulverized seeds are used in spermatorrhea (excessive accidental ejaculation) and found to serve as an aphrodisiac (increases sexual desire) when used along with dry *Zingiber officinale* and milk.

Chinese Herbal Medicine—This is one of the most rich and widely cultivated form of traditional medicine that also finds use of *Vitex negundo* from remote past. This Chinese Pharmacopoeia prescribes the fruits of the plant in the treatment of reddened, painful, and inflated eyes, headache and arthritic joints [43].

Folk Medicine: Folklore systems of medicine in the region of Indian subcontinent and Africa continue to serve a large segment of rural population, especially those in tribal areas, regardless of the introduction of modern medicines [44]. **Table 2** and **Table 3** show the varied use of *Vitex negundo* as folk medicine along with its ethnobotanical diversity and ubiquity.

Pharmacological Studies: The entire plant is used for medicinal purposes. The leaves are astringent, febrifuge (reduces fever), sedative, stimulant, vermifuge (expels intestinal worms) and used to reduce severe pain in rheumatic joints. The extract of the leaves is utilized for insecticidal activity, removing foetid (offensively malodor-

Table 2. Uses of Vitex negundo in folk medicine in India.

State	Region	Local name	Used in the treatment of	Reference
	Puttaparthy	Tella vavilli	Asthma, cancer	[45]
Andhra Pradesh			Used as bath for women in puerperal state and for new born children	Unpublished
			Jaundice	[46]
Assam	-	Pochatia	Urticaria, cellulitis, abcesses, carbuncles, eczema	[47]
			Liver disorders	[48]
Himachal Pradesh	Garhwal	Sambhalu	Kwashiorkor	[1]
riillaciiai Frauesii	Parvati Valley	Bana	Wounds, body ache	[49]
	Dharwad	Lakki, Karilakki	Toothache	[50]
Karnataka	Mysore	Bilenekki	Febrile, catarrhal and rheumatic afflictions	[1]
	Uttara Kanada	Nekki	Migraine	[51]
	Konkan Lingur Rheumatism	Rheumatism	[1]	
Maharashtra	Amaravati	Samhalu	Encephalitis	[52]
	Chota Nagpur	Nirgundi	Expectorant	[1]
	Satpura	Nirgundi Joint ache		[44]
Odisha	Malkangiri	Languni	Jaundice	[53]
	Southern parts Notchi,		Antidote for snake bite	[54]
Tamil Nadu	Madurai	Chinduvaram,		[55]
	Kanchipuram	Nirnochchi, Nochchi,	Respiratory disorders, fever, headache	[56]
	Salem and Tiruchirapalli	Vellai-nochchi		[57]
Uttar Pradesh	Jaunsar-Bawar Hills	Somi	Eye pain	[58]
	Moradabad	Mala	Refrigerant for cattle	[59]
	Uttaranchal	-	48 different types of ailments	[60]

Table 3. Uses of Vitex negundo in folk medicine outside India.

Country	Region	Local name	Used in the treatment of	Reference
Bangladesh	Chitagong	Nishinda	Weakness, headache, vomiting, malaria, black fever	[61]
China	Guangdong	Muching, Huangjing	Common cold, flu and cough	[62]
Nepal	Kali, Gandaki	Simali	Sinusitis, whooping cough	[63]
Pakistan	Buner	Marvandaey	Chest-pain, backache used as toothbrush	[64]
	Kot Manzaray Baba Valley	Sambhalu	Used as anti-allergenic agent	[65]
	Margallah hills	Nirgud	Gum and skin diseases	[66]
	Siran valley	Kalgari	Used as medicine for buffaloes in colic	[67]
Phillipines	-	Lagundi	A number of ailments including cancer	[68]
Sri Lanka	-	Nika	Eye disease, toothache, rheumatism used as a tonic, carminative and vermifuge	[1]

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Entry	Ailments	Reference
1	Anti-inflammatory, analgesic and anti-rheumatic activity: detailed studies have established anti-inflammatory properties of <i>Vitex negundo</i> extracts in acute and sub-acute inflammation. Anti-inflammatory and pain suppressing activities of fresh leaves of the plant are attributed to prostaglandin synthesis inhibition, antihistamine, membrane stabilizing and antioxidant activities.	[69]-[80]
2	Antioxidant activity: leaf extracts of <i>Vitex negundo</i> were determined to possess anti-oxidant potential. The extracts were found to be useful in decreasing levels of superoxide dismutase, catalase and glutathione peroxidase in Freund's adjuvant induced arthritic-rats [82]. This extract also possess the ability to fight oxidative stress by reducing lipid peroxidation because of the presence of flavones, vitamin C and carotene [83]. Rooban [84] measured the antioxidant and therapeutic potential of <i>Vitex negundo</i> flavonoids in modulating solenoid-induced cataract and found it to be effective.	[81]-[85]
3	Enzyme inhibitory activity: root extracts of <i>Vitex negundo</i> showed inhibitory activity against enzymes such as lipoxygenase butyryl-cholinesterase, α -chymotrypsin, xanthine-oxidase, tyrosinase. HIV type 1 reverse transcriptase inhibitory activity of the aqueous extract of the aerial parts of <i>Vitex negundo</i> has also been reported [90].	[24] [86]-[90]
4	Antimicrobial activity: this was assessed using the minimum inhibitory concentration assay. Through bioactivity-guided fractionation, the fraction responsible for the antimicrobial activity was determined. The toxicity profile, anti-oxidant and anti-inflammatory activity was evaluated using the tetrazolium cellular viability, 2,2-diphenyl-1-picrylhydrazyl and 5-lipoxygenase assays respectively. The antimalarial activity of the extracts and isolated compound was also investigated on the chloroquine-resistant gambian FCR-3 strain of <i>Plasmodium falciparum</i> using the tritiated hypoxanthine incorporation assay.	[78] [91]
5	Histomorphological and cytotoxic effects: histomorphological study of <i>Vitex negundo</i> in mice reveals that the stomach tissue to be unaffected even by toxic doses while dose-dependent changes were observed in the heart, liver and lung tissues. Cytotoxic effect of leaf extracts of <i>Vitex negundo</i> was tested and affirmed using COLO-320 tumour cells. It was also observed that the chloroform extracts of <i>Vitex negundo</i> leaves to be toxic to a human cancer cell line panel while on the other hand there are remark that <i>Vitex negundo</i> extracts were non-cytotoxic on mammary and genito-urinary cells of mice.	[70] [92]-[94]
6	Antinociceptive (reducing sensitivity to painful stimuli) activity: tail flick test in rats and acetic acid induced writhing in mice were in use to study the antinociceptive activity of <i>Vitex negundo</i> leaf extract which propose that this plant possesses both central and peripheral analgesic activity. The central analgesic action does not seem to be mediated through opioid receptors.	[78] & references cited therein
7	Drug potentiating activity: it has been found that <i>Vitex negundo</i> extracts potentiated the result of commonly used anti-inflammatory drugs <i>viz.</i> , ibuprofen and phenylbutazone, analgesics such as meperidine, aspirin, morphine and pethidine sedative-hypnotic drugs like pentobarbitone, diazepam and chlorpromazine anti-convulsive drugs like diphenylhydantoin and valporic acid.	[74] [79] [95] [96]
8	Effect on reproductive ability: the flavonoid rich fraction of seeds of <i>Vitex negundo</i> caused disruption of the latter stages of spermatogenesis in dogs and interfered with male reproductive function in rats. It must however be noted that these findings are in sharp contrast with the traditional use of <i>Vitex negundo</i> as aphrodisiac. Hu <i>et al.</i> [73] determined that ethanolic extracts of <i>Vitex negundo</i> showed estrogen-like activity and propounded its use in hormone replacement therapy.	[42] [97]-[99]
9	Anticonvulsant (prevents intense, violent and uncontrolled muscular contractions) activity: mainly the leaf extracts of the plant showed anticonvulsant activities. The root extracts in petroleum provides protection against Leptazole induced convulsions whereas methanolic extracts of the leaves furnished significant protection against Strychnine and Leptazole induced convulsions. The leaves of <i>Vitex negundo</i> also have shown ability to potentiate the effects of standard anticonvulsants.	[79] [80] [95] [100] [101]
10	Antifungal activity: Vitex negundo has been found to highly effective against the fungus Altenaria alternate, Curvularia lunata, Trichophyton mentagrophytes, Cryptococcus neoformans, Aspergillus niger, Candida albicans, Fusarium solani, Microsporum canis etc.	[102]-[104]
11	Anti-tumor and anticancer activity: It is found that the methanol extract of <i>Vitex negundo</i> showed outstanding antitumor activity in a concentration-dependent approach across all the <i>Agrobacterium</i> strains in the potato disc bioassay. This result is in accordance with previous findings, where researchers observed significant antitumor activity of ethanolic leaf extract against Dalton's ascitic lymphoma in Swiss Albino mice [106] [107].	[105]-[107]

Continued

12	Laxative activity: water extract of <i>Vitex negundo</i> showed significant and dose dependant increase in faecal output of rats at selected dose levels. Researchers endorsed anthracene derivatives to be responsible for such findings.	[108]
13	Antidiabetic activity: extracts of <i>Vitex negundo</i> leaves were found to inhibit the catalytic activity of α -amylase which is known to catalyze the hydrolysis of α -1,4-glycosidic linkages of starch, glycogen and various oligosaccharides. The findings are claimed to be significant.	[109]
14	Insecticidal activity: <i>Vitex negundo</i> show potent insecticidal activity against a number of insects such as <i>Collosobruchus maculates</i> (Pulse beetle), <i>Phthorimaea aperculella</i> (Potato-tuber moth), <i>Sitotroga cerealella</i> (Angoumois grain moth), <i>Aphis citricola</i> (Spirea aphid), <i>Aphis gossypii</i> (Melon or cotton aphid), <i>Myzus persicae</i> (Green peach aphid) etc.	[110]-[115]
15	Hepatoprotective activity: leaf extract of <i>Vitex negundo</i> were found to possess hepatoprotective activity against liver damage induced by d-galactosamine, commonly used tubercular drugs and carbon tetrachloride.	[116]-[119]
16	Antileishmanial acivity: luteolin, obtained from <i>Vitex negundo</i> has been observed as a promising antileishmanial agent.	[120]
17	Vitex negundo have also been found to be sufficiently active as an antifeedant (e.g., Spodoptera litura—Asian army worm, Achoea janata—Castor semi-looper), antifilarial (Brugia malayi—Microfilarial parasite), antilarval (Cnaphalocrocis medinalis—Rice leaf-folder), antiviral (Plasmodium falciperum), larvicidal (Anopheles subpictus—Mosquito, Culex tritaeniorhynchus—Mosquito, Culex quinquefasciatus—Mosquito, Anopheles stephensi—Mosquito, Plutella xylostelle—Diamond-back moth) and mosquito repellant (Culex tritaeniorhynchus—Mosquito, Aedes aegypti—Mosquito etc).	[110] & references cited therein

ous) discharges and worms from ulcers, while oil prepared from the leaf juice is applied to sinuses and scrofulous (tuberculous infection of the lymph nodes) sores. The dried fruit is vermifuge and used in treatment of angina (severe pain mainly in chest, also to shoulders, arms and neck owing to an inadequate blood supply to the heart), colds, coughs, rheumatic difficulties etc.

The fresh fruits are crushed to a pulp and used in the form of a tincture for the relief of paralysis, pains in the limbs, weakness etc. The root is expectorant (promotes secretion of sputum by the air passages to treat coughs etc), febrifuge and tonic and used to cure colds and rheumatic ailments. The plant is said to be a malarial preventive and is also used in the treatment of bacterial dysentery. The extracts of the leaves have also shown antimicrobial and antitumor activities. The leaves are used to repel insects in grain stores. The fresh leaves are burnt with grass as a fumigant against mosquitoes. A decoction of the stems is used in the treatment of burns and scalds (burn caused by boiling water).

Some important pharmacological evidences are shown below, in Table 4, citing their relevant references.

6. Conclusion

A popular quote [121] of the Western Himalayas says that a man can not die of disease in a region where *Vitex negundo*, *Adhatoda vasica* and *Acorus calamus* are found, obviously, if he knows appropriate usage of the plants. Even in the Indian traditional community, *Vitex negundo* is uttered as "sarvaroganivarini" [122], the remedy for all diseases. A large inventory of literature is available regarding this plant that includes traditional, biochemical, ethnobotanical and pharmacological experiments, observations and inferences. However, there may have certain miscommunications which must be properly addressed by contemporary researchers. One must make the best use of the naturally available resources which provide invaluable raw materials for advancement of research and knowledge. Nature always put some good lessons in front of us and in due course of time. It is our responsibility to become eligible and compatible with the plethora of resources of knowledge of the present times to combat anything undesired and unnatural.

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