



## A Review of "*Narcissus tazetta* L." in Traditional Persian Medicine and Modern Medicine

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### Abstract

*Narcissus tazetta* L., commonly known as narcissus, is a member of the Amaryllidaceae family. It has a wide distribution worldwide. Various ancient sources, including traditional Persian medicine, Unani medicine, Ayurveda, and Chinese medicine, have documented diverse and significant uses of this plant. Recent studies have also confirmed several pharmacological effects of narcissus. Our aim was to review the references about narcissus in Traditional Persian Medicine (TPM) and compare them with conventional sources. For this purpose, TPM data were extracted from Persian medicine sources; while modern data were obtained from electronic databases such as PubMed, Google Scholar, and SID. TPM sources attribute various effects to narcissus, including treatment of swellings and masses, alleviating pain, and healing of internal and external ulcers. These properties align with the antimicrobial, anticancer, and anti-aging effects reported in recent studies. The integration of ancient knowledge and modern scientific research holds promise in identifying new pharmaceutical and therapeutic approaches. Nevertheless, further studies are needed to comprehend the precise mechanisms of these effects and potential side effects.

**Keywords:** *Narcissus tazetta*; Amaryllidaceae; Persian Medicine; Iranian traditional medicine; Therapeutic

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## Introduction

*Narcissus tazetta* L., belonging to the Amaryllidaceae family and the genus *Narcissus*, is a geophyte, monocotyledonous, and perennial plant. It is a hybrid plant and has about 65 species and 20,000 varieties [1,2]. In Iran, the predominant self-growing bulb is *N. tazetta*, commonly named "Narges" in the region [3]. Morphologically, it is a bulbous plant with a short and thick underground stem measuring 3-5 cm. The stem is covered with scale-like structures, and long leaves emerge from the bulb along with cylindrical stems bearing flowers. The plant's height ranges from 15-45 cm, and its umbellate inflorescence carries approximately 2 to a maximum of 15 flowers [2, 4]. The petals are white to cream-colored and egg-shaped, accompanied by a yellow to orange crown in the center. The flower's trumpet-shaped crown protruding above the petals is referred to as the trumpet, while a crown at the same level as the petals is known as the cup [5]. The fruit of *N. tazetta* is an oval capsule containing spherical, shiny, and black seeds [2].

In traditional Persian medicine (TPM) sources, "Narges" (*N. tazetta*) is described as a plant with smaller and narrower leaves compared to *Gandana* (*Allium ampeloprasum* L.). It possesses a hollow stem and a bulbous root [6]. Additionally, *N. tazetta* shows two growth patterns: wild and cultivated. Wild-growth plants tend to have a more pronounced and robust fragrance [7]. Insects are the primary pollinators of *N. tazetta*, which is a plant that flourishes globally. It is indigenous to Mediterranean regions with an altitude of less than 2000 meters, where winters are wet and summers are hot and dry. In Iran, its habitat is dispersed throughout southern regions from east to west, as well as in the north [1]. The flowering period of *N. tazetta* extends from mid-December to early April, with the peak bloom occurring in January and February [2,8,9]. Given the spread of narcissus in Iran and globally, the continuous need to discover, examine, and apply new drugs, and the cultural significance of the narcissus flower in Iranian culture, we will present the first detailed report on the medicinal and therapeutic effects of narcissus from the perspective of ancient Iranian physicians, and along with it, we will also discuss new discoveries.

## Materials and Methods

The present study employed a literature research approach to investigate key Persian medical and pharmaceutical manuscripts. The following manuscripts were primarily examined: "*Al-Qanun fi al-Tibb*" (The Canon of Medicine) by Avicenna, "*Al-Hawi fi al-Tibb*" by Rhazes, "*Tohfah al Moemenin*" by Mohammad Tonkaboni, and "*Makhzan-al-advieh*" (Storehouse of Medicaments) by Aghili Khorasani. These manuscripts serve as authoritative traditional references in Persian

medicine. The terms "Narges", "Narjes", and "Narcissus" mentioned in the aforementioned manuscripts were specifically investigated. Information regarding the plant's nature, botanical properties, and therapeutic uses was collected from these sources. In order to link traditional knowledge with modern discoveries, additional research was carried out using specific keywords such as "*Narcissus tazetta*", "narcissus" or "Amaryllidaceae" in the title or abstract of articles from PubMed, Google Scholar, and SID. Relevant literature was collected and screened until January 2023.

## Results and Discussion

### Historical Review

*Narcissus tazetta* is a plant with a rich history spanning thousands of years. In ancient Persia, this beautiful and fragrant plant was known as "Narges" and "Narkis" in the Pahlavi language. *Narcissus* is frequently used in similes and literary metaphors [8]. In Greek, it is called "Linus," in French "Narcisse," in English "Narcissus," and in Indian languages "Nargis," while



**Figure 1.** Painting of narcissus (by the first author of this article), Tehran, Iran.

other names like "Abhar", "Arar", and "Susan Narjes" are also mentioned in ancient texts. "Narjes" represents the Arabic form of the Persian word "Narges". Arabs refer to it as "Ayun" and "Tafatih", and its bud is known as "Gahd," [6,10]. Its medicinal properties have been mentioned in ancient texts by renowned figures such as Hippocrates, the father of medicine (460-375 BC) [11], Dioscorides (1<sup>st</sup> AD) [12], and Pliny in his work "Natural History" (23-79 AD) [13]. Dioscorides, referring to it as "Narkissos," acknowledges it as a flower recognized by most people and proceeds to describe the plant and its therapeutic applications [12]. Narratives describe the miraculous growth of Narcissus's flowers by God's command at the place where fire touched Prophet Ibrahim [14]. There are medicinal prescriptions in TPM manuscripts attributed to Galen, Hippocrates [15], and Gabriel Bokhtishua (8-9 AD) [16] about the use of narcissus in the treatment of diseases. Also TPM books like "*Al-Qanun fi al-Tibb*" by Avicenna and "*Al-Hawi fi al-Tibb*" by Rhazes have discussed its botanical and therapeutic properties, and all of them align with the scientific name of the genus "*Narcissus*" as found in conventional sources [17]. The cultivation of this plant is documented in the 16<sup>th</sup> century AD in "Ershad al-Zerae" book [18].

### *Temperament (mezaj) of Narcissus in Traditional Persian Medicine*

According to numerous ancient sources, the temperament of narcissus is described as warm, ranging from the second to the third degree, and dry in the first degree. It was traditionally believed that narcissus oil exhibited a balanced temperament in terms of hotness and coldness. The seeds were perceived to possess hot and dry qualities, with a classification of up to the third degree [19,20].

### *Pharmaceutical dosage forms in Traditional Persian Medicine*

New studies have been conducted on *N. tazetta*, investigating the potential of extracting from flowers, aerial parts, or bulbs [21]. However, ancient Persian texts have documented different ways of using each part of the narcissus, even the seeds (individually or in combination with other components), and diverse preparation methods for them. Traditional and modern dosage forms of narcissus are as follow: "*Shamum*" (Smelling), "*Tadhin*" (Anointing), "*Zemad*" (Poultice or Ointment), "*Farzajah*" (Vaginal Suppository), "*Ta-bikh*" (Decoction), "*Zaroor*" (Topical powder) ,and "*Tela*" (Liniment) [16,19,22].

### *Therapeutic effects in Persian Medicine*

According to TPM, narcissus has several therapeutic functions. These include dissolving of swelling and masses, promoting the healing of internal and external

ulcers, facilitating wound closure, as a pain reliever, inducing emesis, abortifacient properties, anthelmintic activity, and acting as an aphrodisiac [19,21,22,25,27].

### *Side effects and modifiers in Traditional Persian Medicine*

Because of the warm nature of narcissus, it has been identified as potentially harmful for individuals with warm temperament, and its modifiers are considered to be violet and camphor [16].

### *Dosage*

According to TPM sources, the recommended oral dosage is approximately up to 6.8 grams [19].

### *Chemical compounds*

Studies have reported essential oil, alkaloids, amino acids, flavonoids, tannins, terpenoids, steroids, cardiac glycosides, and saponins from chemical analysis of *N. tazetta*, [28,29]. Alkaloids, as secondary metabolites, are the important ingredients of the Amaryllidaceae family. They are highly valuable chemical compounds because they cannot be chemically synthesized [4]. They contain at least one nitrogen atom in their heterocyclic ring. As briefly, secondary metabolites have three functions in plants: 1- Defense mechanisms that help protect plants from herbivores, microorganisms, and other plants. They can act as repellents, deterrents, and even toxicity to ward off insects and vertebrates and compete with other plants (inhibiting seed germination and growth of seedlings) 2- Attraction in order to pollination with emitting fragrance and color 3- UV protection and scavenging radicals [30]. Some of Amaryllidaceae alkaloids isolated from *N. tazetta* are: Lycorine, Pseudolycorine, Galantamine, 11-Hydroxygalantamine, 9-O-methylepseudolycorine, Narcissidine, Pancratidine, 9-O-demethyle-2- $\alpha$ -hydroxyhomolycorine, Haemanthamine, Tazettine, and Ismine [4,31]. Alkaloids, while they possess toxic properties for humans, are intriguing due to their biological effects, that has resulted in their utilization in various fields, including pharmaceuticals, agrochemicals, biopesticides, fragrances, flavors, and food additives [4,30,32].

### **Pharmacological Effects**

#### *Anticholinergic effect*

Some of the *N. tazetta* alkaloids exhibit an inhibitory effect on acetyl-cholinesterase, which leads to nicotinic receptors stimulation and enhances memory function. Galantamine, specifically, has demonstrated its efficacy in memory improvement by increasing acetylcholine levels within the hippocampus. Galantamine crosses the blood-brain barrier, and affects the central nervous system [31,33,34,35]. Acetylcholinesterase inhibitors are the first drugs approved for mild

**Table 1.** Uses of "*Narcissus tazetta*" in Persian Medicine

Part	Dosage form	Usage
Flower	Smelling	Constantly smelling narcissus flowers prevents colds [16]. The power of dilution of thick humor and resolvent property in its aroma is effective for phlegmatic and melancholic headaches, clearing brain blockages, and relieving nasal and pharyngeal discharges [19, 20,23]
	Poultice	A flower poultice is used for dandruff and prevention of nasal and pharyngeal discharges [19]
	Oil	To prepare the oil, narcissus petals are soaked in olive oil and exposed to the sunlight for forty days; the flowers are regularly renewed with new ones and it can be used after this time, or the mixture of oil and flowers is set on a gentle fire so that, the water slowly evaporates, but the oil remains and does not burn [24]. The oil attenuates and dissolves excess brain phlegm humor ( <i>Balgham</i> ), which is one of the four humors as the concept of Persian medicine [20]. It unblocks brain obstructions and is helpful for phlegmatic and melancholic headaches [19,25]. Continuous anointing and perspiration with narcissus oil have been considered helpful for neurotic pain and paralysis caused by " <i>Balgham</i> ". It has been stated that the oil is useful for uterine and bladder pains caused by coldness. It dissolves inflammations caused by coldness [26]. Anointing the chest with narcissus oil dissolves hard and cold swellings ( <i>Oram-e-Solb</i> ) of the diaphragm [25]
Bulb	Powder form	A sprinkle of dried and grated bulb removes the redness and itching of the eyes ( <i>Sabal</i> ) and pterygium and stops bleeding of injuries [19]
	Poultice	Especially with vinegar, it is recommended for the removal of freckles ( <i>Kalaf</i> ), pityriasis ( <i>Bahaq</i> ), and alopecia areata ( <i>Dao-saalab</i> ). The poultice with honey is useful for chronic neurotic pains, joint pains, gout disease, and fractures, and it is also used for fire burns. Its poultice with honey and vinegar ameliorates large and deep wounds, even cuts of tendons, ligaments, and nerves due to its purifying, deterging, and deteriorating of exudates. It can repair the edges of the wound. The poultice with honey and <i>Vicia ervilia</i> (L.) Willd. ( <i>Karsana</i> ), results in the maturation and opening of the large swellings. The poultice of narcissus bulb mixed with <i>Pterocarpus santalinus</i> L.f. ( <i>red Sandalwood</i> ), Armenia clay, <i>Areca catechu</i> L. ( <i>Fofel</i> ), <i>Robinia pseudoacacia</i> L. ( <i>Acaqia</i> ), <i>Lycium barbarum</i> L. ( <i>Hozoz</i> ), lead oxide ( <i>Sefidab and Mordasang</i> ) was used for solid tumors [7,19,25,26]
	Vaginal suppository	Vaginal suppositories prepared from its bulb are emmenagogue, abortifacient and cleanse the uterus [16]
	Decoction	Drinking grated bulb juice or cooked bulb juice is vomituous, especially with honey. It cleans the stomach, uterus and expels live and dead embryos, and heals internal and external ulcers. It is anthelmintic and relieves bladder and uterus pains [7,19,25,26]
	Liniment	Soaked bulb in milk is aphrodisiac in topical use [7,19]
Seeds	Topical mask	Pulverized seeds mixed with vinegar will remove freckles ( <i>Kalaf</i> ) and pityriasis ( <i>Bahaq</i> ) [7]

to moderately severe Alzheimer's disease [28,36]. A dose of 8 mg/kg of *N. tazetta* bulb extract in male Wistar rats led to the recovery of memory destroyed by ethanol [37].

#### *Anticancer effects*

The identification of growth inhibitory compounds in narcissus plants can be traced back to the observations made by farmers. They noticed that the mucilage released from bulb cuts prevents germination [38]. Notably, in 1958, Fitzgerald and his colleagues were the first to discover the antimetabolic effects of alkaloids

extracted from various Amaryllidaceae bulb species [39]. In 1988, a study demonstrated that narciclazine derived from the mucilage of *N. tazetta* bulbs inhibited the germination and growth of rice and cabbage seeds [40]. Furthermore, a glutamine-rich peptide from *N. tazetta* var. *chinensis* exhibited immunomodulatory effects by stimulating splenocytes and bone marrow cells while acting as an inhibitory agent in leukemic cells [41]. Several chemical compounds (alkaloid and nonalkaloid extracts) obtained from aerial and bulbous parts of narcissus have shown effectiveness against different cancer cell lines, including



leukemia (HL-60, K562, KT1/A3, A3R) [42,43,44], breast cancer (MCF-7) [42,45], prostate cancer (PC-3M, DU145, LNCaP, and 22RV1) [45,46], hepatocellular carcinoma (HEPG2) [47], melanoma (murine B16 melanoma 4A5 cells) [48], and gastric cancer (BGC-823, SGC-7901, MGC-803, MKN28) [49]. Animal studies have also demonstrated their efficacy against Rauscher leukemia [50], solid lymphosarcoma tumors, and Ehrlich ascites tumors [51]. Mechanistically, these compounds inhibit cell division (antimitotic activity), induce apoptosis through mitochondrial pathways and cell death receptors, and promote apoptosis through autophagy, ultimately leading to a reduced survival rate of tumor cells [35, 49, 52]. In a laboratory experiment, the green synthesis of silver nanoparticles using *N. tazetta* exhibited a decrease in the lifespan of rhabdomyosarcoma cells [53].

#### Antimicrobial effects

The extract of *N. tazetta* aerial part exhibited notable effects against Gram-negative bacterial strains (*Escherichia coli*, *Pseudomonas aeruginosa*), as well as Gram-positive bacterium (Methicillin-Resistant *Staphylococcus aureus* (MRSA), *Salmonella typhimurium*, *Bacillus cereus*, *Pseudomonas aeruginosa*), and fungi (*Candida albicans*, *Aspergillus niger*) at 1 mg/mL concentration [54]. An alkaloid of *N. tazetta* (nartazine) revealed antifungal activity against four phytopathogenic fungi (*Botrytis cinerea*, *Fusarium oxysporum*, *Mycosphaerella arachidicola*, *Physalospora piricola*), also the data exhibited pronounced resistance to proteolytic digestion [41]. The use of silver nanoparticles containing *N. tazetta* extract has had effectiveness in fighting MRSA *in vitro* [53].

#### Antiviral effects

The compounds extracted from *N. tazetta*, particularly its alkaloids, have demonstrated effectiveness against a range of viruses such as *flaviviruses* (*Japanese encephalitis virus*, *dengue virus*, and *yellow fever*), *bunyaviruses*, *alphaviruses*, and *lentiviruses* [55]. Inhibition of viral plaque formation by mannose binding lectin is reported in respiratory syncytial virus (RSV), influenza A (H1N1, H3N2, H5N1), influenza B [56], and bovine rhinotracheitis and equine rhinopneumonitis viruses [57]. The inhibitory effect of narcissus alkaloids on Avian myeloblastosis viruses (AMV) achieved through transcriptional suppression, surpasses that of standard drugs [58]. An ethanolic extract of *N. tazetta* on Vero-E6 cell line identified an effective inhibition of *SARS-CoV-2* replication via a unique mannose binding lectin NTL-125 [59].

#### Antimalarial effects

*N. tazetta* extract exhibited antimalarial activity against the chloroquine-resistant (K1) strain of *Plasmodium falciparum* in an *in vitro* study [37,60,61].

#### Antioxidant effects

A study conducted on *N. tazetta* flower extract revealed the presence of phenolic compounds which demonstrated antioxidant and hepatoprotective effects in cadmium chloride-induced hepatic damage in Swiss albino mice [9]. A study focusing on the glandular part extract of *N. tazetta* exhibited its antioxidant activity against the hydrogen peroxide-induced toxicity in human neuroblastoma cells [62].

#### Dermal effects

Laboratory investigations on human fibroblasts have revealed significantly positive impact of using the bulb of *N. tazetta* on proliferation and wound healing, potentially attributed to its antiviral, antibacterial, antioxidant, and anti-inflammatory mechanisms [63]. Another laboratory study exhibited improvement in skin aging indicators, including reduction of skin folds and lines, pigmentation reduction, increased skin elasticity, and improved the skin barrier function, following the utilization of bulbous extract from *N. tazetta* [64]. Impact of a botanical blend containing *N. tazetta* bulb extract and *Schisandra chinensis* fruit extract on human skin equivalents showed a positive effect on skin health via modulation of gene expression and microRNA [65].

#### Hemodynamic effects

The inhibitory properties of *N. tazetta* extract on platelet aggregation induced by arachidonic acid, collagen, and platelet-activating factor have been documented. Additionally, the extract from *N. tazetta* has demonstrated the ability to inhibit contraction of the rat aorta caused by high potassium and norepinephrine [61]. Upon investigating the bulbar extract of *N. tazetta* in rats, bioactive compounds with significant effects on cardiovascular function were identified, collectively resulting in blood pressure reduction [66].

#### Antinociceptive effect

Antinociceptive effect of ethanolic bulb extract of *N. tazetta* was examined on p-benzoquinone-induced abdominal constriction of male albino mice. Subcutaneous injection of extract at doses of 100.0 and 200.0 mg/kg significantly reduced the number of p-benzoquinone-induced abdominal constrictions; however, it was extremely toxic at the 500.0 mg/kg dose. In the hot plate test (5–500 mg/kg intraperitoneal) extracts had no antinociceptive effect which indicate that the antinociceptive effect is influenced by the pain intervention model [67].

#### Poisoning and side effects

Numerous allergens have been discovered in the *N. tazetta* bulb, which are responsible for the contact dermatitis commonly reported by gardeners. Picking flowers can cause an eczematous or granulomatous

rash on arms, wrists, forearms, chin, and axilla due to sap irritation. The symptoms of mistaking consumption of the plant range from asymptomatic to nausea, vomiting, abdominal pain, diarrhea, and narcosis. Death has also been reported in ingestion of the glandular part [28]. When the plant is ingested, a protein called Narcin A13KDa triggers the production of pro-inflammatory cytokines, particularly IL3 and IL4, leading to allergies, increased levels of IgE, and poisoning. According to a report from the US Poison Control Center in 2011, out of 47,000 cases of plant-related poisonings, less than 1% were attributed to narcissus consumption [68]. A study on male rats examining the effects of high doses (100 mg/kg for 6 days) of an oral alcoholic bulb extract of narcissus on indicators of kidney function observed a decrease in total protein and albumin levels, as well as an increase in urea and creatinine concentrations [29].

## Conclusion

The ancient sages possessed extensive knowledge of the narcissus plant and employed its various parts in different ways, ranging from simply smelling the flowers to using bulb and seeds, either alone or in combination with the other ingredients. Recent studies, primarily conducted in laboratory and animal settings, have revealed numerous valuable pharmacological effects associated with *N. tazetta*, which are largely consistent with the plant's properties and historical uses as described in ancient texts. Its proven antimicrobial, cytotoxic, antioxidant, and memory-enhancing effects are aligned with its traditional uses in the treatment of swelling, masses, wounds, and relief of the pain of some organs in specific conditions, as documented in ancient manuscripts. There appears to be potential for further exploration of narcissus effects in the fields of burns, leishmaniasis, and even diabetic foot ulcers. Also, based on ancient physicians' beliefs regarding the plant's impact on cold-natured pains occurring in the head, uterus, and bladder, conducting more research in these fields may provide new insights into the diverse effects of narcissus. Ultimately, to use the potential medicinal and therapeutic properties of this plant, we need comprehensive studies including cellular, animal, and clinical research.

## Conflict of Interests

None.

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None.

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