

Constituents and pharmacology of *Narcissus tazetta*

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ABSTRACT:

The chemical analysis of *Narcissus tazetta* showed that it contained flavonoids, alkaloids, saponins, tannins, cardiac glycosides, oil, steroids, terpenoids and anthraquinones. The pharmacological investigation showed that *Narcissus tazetta* antibacterial and antifungal, antiviral, antimalarial, anticancer, antioxidant, dermatological, cardiovascular, immunomodulatory and acetylcholinesterase inhibitory effects. The current review discussed the chemical constituents and pharmacological effects of *Narcissus tazetta*.

KEYWORDS: *Narcissus tazetta*, ingredients, pharmacology, therapeutic

I. INTRODUCTION:

Medicinal plants are the Nature's gift to human beings to help them pursue a disease-free healthy life. Plants have been used as drugs by humans since thousands of years ago. As a result of accumulated experience from the past generations, today, all the world's cultures have an extensive knowledge of herbal medicine. Two thirds of the new chemicals identified yearly were extracted from higher plants. 75% of the world's population used plants for therapy and prevention. In the US, where chemical synthesis dominates the pharmaceutical industry, 25% of the pharmaceuticals are based on plant-derived chemicals⁽¹⁾. Plants are a valuable source of a wide range of secondary metabolites, which are used as pharmaceuticals, agrochemicals, flavours, fragrances, colours, biopesticides and food additives⁽²⁻²¹⁾. The chemical analysis of *Narcissus tazetta* showed that it contained flavonoids, alkaloids, saponins, tannins, cardiac glycosides, oil, steroids, terpenoids and anthraquinones. The pharmacological investigation showed that *Narcissus tazetta* antibacterial and antifungal, antiviral, antimalarial, anticancer, antioxidant, dermatological, cardiovascular, immunomodulatory and acetylcholinesterase inhibitory effects. The current review was designed to discuss the chemical constituents and pharmacological effects of *Narcissus tazetta*.

II. SYNONYMS:

Hermione ambigena, *Hermione amoena*, *Hermione antipolensis*, *Hermione aperticorona*, *Hermione auranticorona*, *Hermione biancae*, *Hermione breviflora*, *Hermione brevistyla*, *Hermione callichroa*, *Hermione calliopsis*, *Hermione cerina*, *Hermione cheiranthea*, *Hermione chrysantha*, *Hermione citrine*, *Hermione contorta*, *Hermione corrugate*, *Hermione crenularis*, *Hermione crenulata*, *Hermione crispicorona*, *Hermione cypri*, *Hermione debilis*, *Hermione decora*, *Hermione deflexicaulis*, *Hermione discolor*, *Hermione discrete*, *Hermione erodora*, *Hermione fistulosa*, *Hermione flaveola*, *Hermione flexiflora*, *Hermione floribunda*, *Hermione floslactis*, *Hermione Formosa*, *Hermione formosissima*, *Hermione fulgida*, *Hermione ganymedoides*, *Hermione grandicrenata*, *Hermione grandiflora*, *Hermione hololeuca*, *Hermione insolita*, *Hermione intermedia*, *Hermione italica*, *Hermione jucunda*, *Hermione latifolia*, *Hermione leucojifolia*, *Hermione littoralis*, *Hermione lobata*, *Hermione luna*, *Hermione lutea*, *Hermione luteola*, *Hermione mediterranea*, *Hermione modesta*, *Hermione monspeliensis*, *Hermione multiflora* var. *aurantia*, *Hermione neapolitana*, *Hermione neglecta*, *Hermione nobilis*, *Hermione ochroleuca*, *Hermione pallid*, *Hermione patula*, *Hermione perlutea*, *Hermione polyantha*, *Hermione praecox*, *Hermione sequentis*, *Hermione sertulosa*, *Hermione sexlobata*, *Hermione solaris*, *Hermione splendens*, *Hermione straminea*, *Hermione stylosa*, *Hermione subalbida*, *Hermione subcrenata*, *Hermione sublutea*, *Hermione sulcicaulis*, *Hermione sulphurea*, *Hermione syracusana*, *Hermione tazetta*, *Hermione tenuiflora*, *Hermione tereticaulis*, *Hermione trewiana*, *Hermione trifida*, *Hermione tubulosa*, *Hermione unicolor*, *Hermione venusta*, *Hermione virginea*, *Jonquillatazetta*, *Narcissus bicrenatus*, *Narcissus biscrenatus*, *Narcissus breviflorus*, *Narcissus canaliculatus*, *Narcissus cerinus*, *Narcissus citrinus*, *Narcissus commutatus*, *Narcissus cypri*, *Narcissus deflexicaulis*, *Narcissus elatus*, *Narcissus etruscus*, *Narcissus fistulosus*, *Narcissus flos-lactis*, *Narcissus ganymedoides*, *Narcissus leucojifolius*, *Narcissus linnaeanus* var. *antipolensis*, *Narcissus linnaeanus* subsp. *ganymedoides*, *Narcissus neglectus*, *Narcissus neglectus* var. *commutatus*, *Narcissus orientalis*, *Narcissus papyraceus* var. *sequentis*, *Narcissus patulus*, *Narcissus patulus* subsp. *etruscus*, *Narcissus patulus* subsp. *ricasolianus*, *Narcissus patulus* subsp.

siculus, *Narcissus patulus* var. *timbalii*, *Narcissus patulus* subsp. *vergellensis*, *Narcissus puccinellii*, *Narcissus ricasolianus*, *Narcissus sexlobatus*, *Narcissus siculus*, *Narcissus spathulatus*, *Narcissus stramineus*, *Narcissus syriacus*, *Narcissus tazetta* subsp. *canaliculatus*, *Narcissus tazetta* var. *cyprici*, *Narcissus tazetta* subsp. *cyprici*, *Narcissus tazetta* subsp. *eutazetta*, *Narcissus tazetta* var. *mediterraneus*, *Narcissus tazetta* var. *orientalis*, *Narcissus tazetta* subsp. *patulus*, *Narcissus tazetta* var. *syriacus*, *Narcissus tazetta* subsp. *tazetta*, *Narcissus tazetta* var. *varians*, *Narcissus tazettus*, *Narcissus timbalii*, *Narcissus trewianus*, *Narcissus varians*, *Narcissus vergellensis*, *Pancreatium tazetta*, *Queltia orientalis*, *Schisanthes orientalis*⁽²²⁾.

Taxonomic classification:

Kingdom: Plantae, **Subkingdom:** Viridiplantae, **Infrakingdom:** Streptophyta, **Superdivision:** Embryophyta, **Division:** Tracheophyta, **Subdivision:** Spermatophytina, **Class:** Magnoliopsida, **Superorder:** Lilianae, **Order:** Asparagales, **Family:** Amaryllidaceae, **Genus:** *Narcissus*, **Species:** *Narcissus tazetta*⁽²³⁾.

Common names:

Arabic: nargis, **English:** bunchflower daffodil, bunchflower narcissi, Chinese sacred-lily, daffodil, polyanthus narcissus, tazetta; **Portuguese:** narciso; **Swedish:** tazett⁽²⁴⁾.

Distribution:

Narcissus tazetta is a widespread species, native from the Mediterranean region, distributed in **Africa** (Algeria, Egypt, Libya, Morocco); **Asia** (Iran, Iraq, Palestine, Jordan, Lebanon, Syria, Turkey, Russian Federation-Ciscaucasia, Russian Federation-Western Siberia, China); **Europe** (Russian Federation-European part, Albania, Former Yugoslavia, Greece, Italy, France, Portugal, Spain) and cultivated in wide areas in the world⁽²⁴⁾.

Description:

Narcissus tazetta is a perennial ornamental plant that grows from a bulb. Bulbs ovoid, 4–6 × 3–5 cm, tunic pale to dark brown. Leaves 4; blade flat, 25–35 cm × 8–15(–20) mm, glaucous. Inflorescences umbellate, 5–15-flowered, 25–35 cm; spathe pale brown, 4–6 cm, papery. Flowers strongly fragrant; perianth 2–4 cm wide, perianth tube 1.5–2 cm, gradually tapering to base; distinct portions of tepals spreading to reflexed, white to cream, linear-ovate to oblanceolate, 1–2 × 0.5–1 cm, apex acute; corona yellow, cup-shaped, 3–5 × 5–10 mm, apex crenulate to ruffled; 3 shorter stamens included within perianth tube, 3 longer stamens and style exerted into mouth of corona; pedicel of variable length, to 8 cm. 2n = 22⁽²⁵⁾.

Traditional uses:

Narcissus tazetta was used in the treatment of Alopecia areate, for the prevention and treatment of damaged skin resulting from conditions like acne vulgaris, atopic dermatitis, alopecia, vitiligo, pruritus, eczema, etc. An essential oil obtained from the flowers was used in perfumery⁽²⁶⁻²⁷⁾.

It was said that the plant possessed emetic, cathartic, antispasmodic, and narcotic properties. It was used in epilepsy, in hysteria, and other spasmodic affections⁽²⁸⁾.

The root was used to relieve headaches. The chopped root was applied externally as an antiphlogistic and analgesic poultice in abscesses, boils and other skin complaints⁽²⁹⁻³⁰⁾. In Jordan, the infusion of the aerial parts and flowers were used as anticancer, antiinflammatory, memorigenic, and sedative⁽³¹⁾. The Bulbs of *Narcissus tazetta* was used for the treatment of breast cancer⁽³²⁾.

Parts used medicinally:

Flowers and bulbs of the plant were used medicinally⁽²⁹⁻³⁰⁾.

Physicochemical parameters:

Physicochemical analyses showed that the moisture content of the *Narcissus tazetta* bulb was ranged from 74.13±1.16 w/w % in the fresh bulb to 9.9±0.2 w/w % in dried one. Total ash of the plant was 4.9±0.2 w/w% of which 2.46/4.9 ×100 was water soluble and 0.1/4.9 ×100 was acid insoluble ash⁽³³⁾.

Chemical constituents:

The preliminary analysis showed that it contained flavonoids, alkaloids, saponins, tannins, cardiac glycosides, oil, steroids, terpenoids and anthraquinones^(31, 33-35).

The essential oils of the flowers of *Narcissus tazetta* subsp *tazetta* from Greece were composed (%) of: heptanal: 1.15, myrcene: 0.56, 1,8-cineole: 5.88, trans-ocimene: 61.12, linalool: 0.78, nonanal: 0.66, benzyl acetate: 6.04, α-terpineol: 3.37, decanal: 0.39, 2-phenylethyl acetate: 1.16, undecanal: 1.14, 3-phenylpropyl acetate: 6.4, γ-dodecalactone: 1.08, heneicosane: 0.97, tetracosane: 0.66 and pentacosane: 0.45⁽³⁶⁾.

In studying the composition of the oil of *Narcissus tazetta* grown in different soils in Egypt, it was found that α-pinene (22.24%), ethyl cinnamate (15.89%), α-terpineol (14.86%) and linalool (13.42%) represented the major components in the oil of *Narcissus tazetta* grown in loamy soil, while, α-pinene

(15.38%), α -terpinene (15.27%), ethyl cinnamate (13.68%) and linalool (11.60%) were the predominant compounds in the oil of *Narcissus tazetta* grown in new reclaimed sandy soil, and linalool (19.34%), methyl cinnamate (11.91%), ethyl cinnamate (10.61%) and limonene (8.31%) were the major constituents in the sandy soil⁽³⁷⁾.

Volatile components of the single-flowered and double-flowered Chinese *Narcissus tazetta* var. *chinensis* were analyzed by headspace solid-phase microextraction coupled with GC and with GC-MS. Thirty five components were identified in single-flowered samples, including monoterpenes (α -pinene, sabinene, β -pinene, myrcene, α -phellandrene, δ -3-carene, α -terpinene, limonene, (*Z*)- β -ocimene, (*E*)- β -ocimene, γ -terpinene, α -terpinolene, allo-ocimene), three terpene alcohols (linalool, α -terpineol, myrtenol), terpene aldehyde (6-methyl-5-hepten-2-one), terpene esters (geranyl acetate, methyl cinnamate, cinnamyl acetate), terpene oxide (1,8-cineole), aromatic aldehyde, aromatic alcohol (benzyl alcohol), aromatic esters (benzyl acetate, phenethyl acetate, 3-phenylpropyl acetate, benzyl benzoate), sesquiterpene (β -caryophyllene), three aliphatic esters (isoamyl acetate, prenyl acetate, 3-hexenyl acetate), hydrocarbons (pentadecane, eicosane), and other compound (indole). A total of 26 components were identified in double-flowered samples, including 13 monoterpenes, three terpene alcohols, one terpene oxide, one aromatic alcohol, three aromatic esters, two aliphatic esters, two hydrocarbons, and one other compound. The main constituents of the Chinese narcissus flowers were (*E*)- β -ocimene (62.73%–66.06%), benzyl acetate (11.65%–25.02%), (*Z*)- β -ocimene, 1,8-cineole, and linalool⁽³⁸⁾.

Many alkaloids: pretazettine, tazettine, homolycorine, haemanthamine, ismine, narcisine, narciclasine, lycorine, pseudolycorine, pseudolycorine N-oxide, galanthamine, nor-galanthamine, 11-hydroxygalanthine, buphanisine, haemantamine, 3-epihydroxy bulbispermine, *O*-methylmaritidine, 9-*O*-Demethylhomolycorine, 3-epi-hydroxybulbispermine and N-methyl-8,9-methylenedioxy-phenanthridinium were isolated from *Narcissus tazetta*⁽³⁹⁻⁵¹⁾.

The galanthamine content of *Narcissus tazetta* subsp. *tazetta* of Turkish origin was 0.0051% in the bulbs and 0.0055% in the aerial parts of the plant, while, lycorine was determined as 0.0250% in the bulbs and 0.0672% in the aerial parts⁽⁵²⁾.

The amounts of narciclasine in the bulb, leaf, flower, stalk and flower of *Narcissus tazetta*, were 0.20, 0.71, 0.62 and 0.39 μ g/g respectively⁽⁴⁰⁾.

The amount of total flavonoid in the percolation extract of *Narcissus tazetta* bulb was 27.04 \pm 0.93 mg/g and in the sonication extract was 24.80 \pm 1.25 mg/g⁽³³⁾. Flavonoids (rutin, quercetin and kaempferol) and phenolic acids were identified in the extracts of the bulbs of *Narcissus tazetta*^(33, 53-55). Two unusual rearranged flavan derivatives with a rare bicyclo [3.3.1] non-3-ene-2,9-dione ring (tazettone A and tazettone B), were isolated in the bulbs of *Narcissus tazetta* var. *chinensis*⁽⁵⁶⁾.

Eleven compounds: tazettones C-G, (2S)-3',4'-dihydroxy-7-methoxyflavan, (2S)-3',7-dihydroxy-4'-methoxy-8-methylflavan, (2S)-liquiritigenin 7-methyl ether, 8-methylnaringenin, farrerol, and cyrtominetin, were isolated from the bulbs of *Narcissus tazetta* var. *chinensis*⁽⁵⁷⁾.

Four phenylethanoid glycosides, tazettosides A–D, and phenylpropanoid glycoside, tazettoside E were isolated from the methanol extract of the flowers of *Narcissus tazetta* var. *chinensis*⁽⁵⁸⁾.

Naturally acetylated glucomannan with MW 31000 was isolated from bulbs of *Narcissus tazetta*. It contained 12.9% O-Ac groups and consisted of D-mannose and D-glucose in a 1:5.6 ratio⁽⁵⁹⁾.

A mucous polysaccharide, named narcissus-T-glucomannan, was isolated from the bulbs of *Narcissus tazetta* var. *chinensis*. It was composed of D-mannose and D-glucose (63.9 and 12.6% respectively) in the molar ratio of 5 : 1, and its molecular weight was estimated to be 119000⁽³²⁾.

Three lectins with similar N-terminal amino acid sequences were isolated from the bulbs of the Chinese daffodil *Narcissus tazetta*. The lectins were all adsorbed on mannose-agarose and demonstrated a single band with a molecular weight of 13 kDa in SDS-polyacrylamide gel electrophoresis and a single 26 kDa peak in gel filtration, indicating that they were mannose-binding, dimeric proteins⁽⁵³⁾.

A mannose-binding lectin was isolated from leaves of the Chinese daffodil, *Narcissus tazetta*. It was an unglycosylated homodimer with a molecular mass of 26 kDa⁽⁶⁰⁾.

Three mannose-specific lectins (isolectins 1, 2, and 3) were isolated from leaves of the Chinese *Narcissus tazetta*. All three isolectins were homodimers with a molecular weight of 26 kDa⁽⁶¹⁾.

A glutamine-rich peptide, named nartazin, was purified from the bulbs of the Chinese daffodil *Narcissus tazetta* var. *chinensis*. Its molecular mass was 7.1 kDa, as determined by SDS-PAGE and gel filtration. The sequence of its first 20 N-terminal residues was characterized by an abundance of glutamine⁽⁶²⁾.

Pharmacological effects:

Acetylcholinesterase inhibitory activity:

Amaryllidaceae alkaloids and *Narcissus* extracts were used in Alzheimer's disease as inhibitors of acetylcholine esterase. Alkaloids, belonging to the galanthamine and lycorine skeleton types, exhibited the more potent acetylcholine esterase inhibitory effects⁽⁶³⁾.

The *in vitro* anti-acetylcholinesterase (AChE) assay results indicated that the extracts of the bulbs of *Narcissus tazetta* were effective inhibitors for AChE enzyme (100% inhibition at a concentration of 1000 µg/ml, 87.13% at a concentration of 100 µg/ml and 58.23% at a concentration of 10µg/ml). The aerial parts also showed noticeable inhibition on AChE (100% inhibition at a concentration of 1000µg/ml, 67.47 % at a concentration of 100 µg/ml and 30.59% at a concentration of 10µg/ml). Both samples also inhibited butyrylcholinesterase (BuChE), the bulbs of the plant caused (85.23 % inhibition at a concentration of 1000 µg/ml, 37.96% at a concentration of 100 µg/ml and 23.90 % at a concentration of 10µg/ml), while the aerial parts caused (92.67 % inhibition at a concentration of 1000 µg/ml, 35.06 % at a concentration of 100 µg/ml and 11.02 % at a concentration of 10µg/ml)⁽⁶²⁾.

The alkaloids (lycorine, tazettine, N-nor-galanthamine, haemanthamine) and 3-epi-hydroxybulbispermine isolated from *N. tazetta* subsp. *tazetta* were investigated for acetylcholinesterase inhibiting activity at 10 µg/ml concentration. The acetylcholinesterase inhibiting rates were: lycorine 43.69%, tazettine 36.34%, galanthamine 48.00%, 3-epi-hydroxybulbispermine 30.18% N-nor-galanthamine 34.09% and haemanthamine 20.8 %. Chloroform: methanol extract and crude alkaloid extract of the plant were also possessed acetylcholinesterase inhibiting activity (46.62±0.77 and 46.96±0.08%, respectively)⁽⁴⁵⁾.

Antibacterial and antifungal effects:

The antimicrobial activity of the ethanolic extract of the aerial parts of *Narcissus tazetta* was investigated against Gram negative and Gram positive bacteria [*Pseudomonas aeruginosa*, *Escherichia coli*, *Salmonella typhimurium*, *Bacillus cereus*, *S. aureus*(MRSA)] and also against fungi (*Candida albicans* and *Aspergillus niger*). The ethanolic extract (1mg/ml) possessed microbial growth inhibition of 52.23, 44.08, 70.50, 75.93, 48.96, 99.23, 5.69 %, against the tested pathogens, respectively⁽³¹⁾.

The ethanolic extracts of *Narcissus tazetta* ssp. *tazetta* at 200 mg/100 ml concentrations showed antibacterial activity against *Staphylococcus aureus*, *Pseudomonas pseudomolli*, *Vibrio cholerae*, *Enterobactercloacea*, *Corynebacterium hoffmanni*, *C. diptheriae* and *Salmonella typhi*⁽²⁸⁾.

The antibacterial effects of narciclasine isolated from *Narcissus tazetta* were studied against Gram-positive species (*Bacillus cereus* and *Staphylococcus aureus*) and Gram-negative species (*Agrobacterium radiobacter* and *Escherichia coli*). Narciclasine showed no inhibitory effect on the growth of these bacteria species⁽⁴⁰⁾.

A glutamine-rich antifungal peptide (nartazin), purified from the bulbs of the Chinese daffodil *Narcissus tazetta* var. *chinensis*, possessed antifungal activity against four phytopathogenic fungi. Its activity was retained after incubation with bovine trypsin and chymotrypsin (enzyme: substrate ratio 1:10 w/w) at 37C for 1h but was attenuated after treatment with proteinase K⁽⁶²⁾.

Ethanolic extract possessed significant antifungal activity against *Nigrosporaoryzae*, *Microsporium canis*, *Pleuralus ostreatus*, *Curvularia lunata*, *Trichophyton longifusus*, *Drechsleza rostrata*, *Aspergillus niger*, *candida albicans*, and *Alefcheria boydii*⁽²⁸⁾.

Antiviral effects:

An alkaloid extract of the *Narcissus tarzetta*, inhibits the purified DNA polymerase from Avian myeloblastosis virus by a mechanism differed from that of other known inhibitors. The alkaloid extract physically combined with the polymerase, it does not affect the binding of the template to the enzyme. The inhibition was the same whether viral 70S RNA or poly d(AT) was used as template⁽⁶⁴⁾.

A mannose-binding lectin with potent antiviral activity was isolated and purified from the bulbs of the Chinese daffodil *Narcissus tazetta* var. *chinensis*. The isolated mannose-binding lectin significantly inhibited plaque formation by the human respiratory syncytial virus (RSV) with an IC₅₀ of 2.30 microg/ml and exhibited strong antiviral properties against influenza A (H1N1, H3N2, H5N1) and influenza B viruses with IC₅₀ values ranging from 0.20 microg/ml to 1.33 microg/ml in a dose-dependent manner. The modes of antiviral action of mannose-binding lectin against RSV and influenza A virus were significantly different. Mannose-binding lectin was effective in the inhibition of RSV during the whole viral infection cycle, but its antiviral activity was mainly expressed at the early stage of the viral cycle of influenza A (H1N1) virus⁽⁶⁵⁾.

Pseudolycorine alkaloid, isolated from *Narcissus tazetta* was studied as new antiviral agent, it showed a superior prolongation effect on the life span of established Rauscher leukemic mice having palpable splenomegaly, in comparison with standard antileukemic drugs. The alkaloid suppressed the development of splenomegaly and the increase in number of nucleated blood cells, and dropped the virus titer in plasma without apparent toxicity. A second alkaloidal complex, called residual alkaloid, also showed remarkable antileukemic activity⁽⁶⁶⁾.

A series of Amaryllidaceae isoquinoline alkaloids and related synthetic analogues were evaluated in cell culture against the RNA-containing flaviviruses (Japanese encephalitis, yellow fever, and dengue viruses), bunyaviruses (Punta Toro, sandfly fever, and Rift Valley fever viruses), alphavirus (Venezuelan equine encephalomyelitis virus), lentivirus (human immunodeficiency virus-type 1) and the DNA-containing vaccinia

virus. Narciclasine, lycoricidine, pancratistatin, 7-deoxypancratistatin, and acetates 6-8, isonarciclasine, cis-dihydronarciclasine, trans-dihydronarciclasine, their 7-deoxy analogues 13b-15b, lycorines and pretazettine exhibited *in vitro* activity against all the flaviviruses and against the bunyaviruses, Punta Toro and Rift Valley fever virus. However, selectivity of the active compounds was low, with toxicity in uninfected cells (TC₅₀) occurring at concentrations within 10-fold that of the viral inhibitory concentrations (IC₅₀). No activity was observed against human immunodeficiency virus-type 1, Venezuelan equine encephalomyelitis virus, or vaccinia viruses. Pancratistatin and its 7-deoxy analogue 5 were evaluated in two murine Japanese encephalitis mouse models (differing in viral dose challenge, among other factors). In two experiments (low LD₅₀ viral challenge, variant I), prophylactic administration of 4 at 4 and 6 mg/kg/day (2% ethanol/saline, sc, once daily for 7 days) increased survival of Japanese-encephalitis-virus-infected mice to 100% and 90%, respectively⁽⁶⁷⁾. Ethanolic extract of *Narcissus tazetta* bulb elicited antiviral activity (bovine rhinotracheitis and equine rhinopneumonitis viruses) by inhibition of viral plaque formation. *Narcissus tazetta* bulb did not directly inactivate the virus extracellularly. The extract exhibited only limited toxicity to rapidly multiplying bovine endocardial cells at plaque-inhibitory levels and wasn't cytotoxic to preformed confluent cell monolayers⁽⁶⁸⁾.

Anti- Plasmodium effects:

The activity of Amaryllidaceae alkaloids and the extracts of Amaryllidaceae plants was studied *in vitro* against a chloroquine resistant (K1) strain of *Plasmodium falciparum*. The extract of *Narcissus tazetta* ssp. *tazetta*, lycorine, tazettine and galanthamine exhibited antimalarial activity, but, galanthamine showed the least anti- *Plasmodium* activity⁽²⁸⁾.

Four groups of Amaryllidaceae alkaloids: lycorine-, crinine-, tazettine-, and galanthamine-type, as well as plant extracts of the *Narcissus tazetta* ssp. *tazetta* were evaluated for their inhibitory activity against *Plasmodium falciparum* *in vitro*. All four groups of alkaloids exhibited antimalarial activity at different potencies. 6-hydroxyhaemanthamine, haemanthamine and lycorine were found to be the most potent alkaloids against *P. falciparum* (T9.96) and galanthamine, while, tazettine possessed the least potent activity against *P. falciparum* (K1)⁽⁶⁹⁾.

Cytotoxic effects:

The aerial parts extracts of *Narcissus tazetta* possessed *in vitro* anticancer activity against MCF-7 and Hep-2⁽⁷⁰⁾. The cytotoxicity of the ethanolic extract of the aerial parts of *Narcissus tazetta* was investigated against Vero cell line using the MTT assay. The extract possessed cytotoxic effect with IC₅₀ of 131.01 ± 5.20 µg/ml⁽³¹⁾. Two quaternary alkaloids with a phenanthrene skeleton, N-methyl-8,9-methylenedioxy-phenanthridinium methylsulfate and N-methyl-8,9-methylenedioxy-phenanthridinium malate isolated from the polar fraction of an ethanolic extract of the fresh flowers of *Narcissus tazetta* showed cytotoxic activities against a panel of cancer cell lines⁽⁴⁸⁾.

Anticancer activity of the alkaloidal and non-alkaloidal neutral fractions of narcissus bulbs has been demonstrated against Ehrlich ascites tumor and 6C₃HED solid lymphosarcoma cells in mice. The single ip administration of the neutral fraction was enough to eradicate Ehrlich ascites cells in about 50% of mice, while the alkaloidal fraction needed multiple administrations to suppress tumor growth. The residual alkaloid also showed moderate activity against syngeneic MCDV-12 leukemia cells in BALB/c mice⁽⁷¹⁾.

The cytotoxicity and antileukemic activity of numbers of Amaryllidaceae alkaloids with pretazettine, a narcissus alkaloid, were performed on the systems of Rauscher virus-carrier cells and the leukemic mice. Only precriwelline, a stereochemical epimer of pretazettine, was found to be therapeutically active as that of pretazettine. The natural precursors such as haemanthamine, crinamine and 6-hydroxycrinamide were also moderately active, but the artificial final product, tazettine, was inactive. The structure-activity relationship of pretazettine or precriwelline was partially analyzed⁽⁷²⁾.

The cytotoxic effects of Amaryllidaceae alkaloids, belonging to different skeletal types were evaluated against one murine non-tumoral cell line (LMTK) and two human tumoral cell lines (Molt4 and HepG2). Pretazettine was the most active compound among the tested alkaloids on the Molt4 lymphoid cells, but was inactive against HepG2 hepatoma. On the other hand, lycorenine was the most cytotoxic compound against HepG2 hepatoma, even though it appeared to be inactive against Molt 4 cells. Almost all of the tested alkaloids showed cytotoxic activity against fibroblastic LMTK cells, but only mesembrenone showed some specificity against Molt4 cells in comparison to LMTK cells⁽⁷³⁾.

The extract of *Narcissus tazetta* var. *chinensis* strongly decreased the survival rate of many tumor cell lines (HL-60, K562, KT1/A3, and A3R). The cytotoxic effects of the extract on non-cancer cells lines (NHBE and NIH3T3) were smaller than on leukemia cell lines. The extract induced HL-60 cell apoptosis. The mitochondrial pathway and cell death receptor pathway were both involved in the apoptosis signal pathways induced by the extract. Upregulation of Bax showed that the Bcl-2 family was involved in the control of apoptosis⁽⁷⁴⁾.

Nartazin, purified from the bulbs of the Chinese daffodil *Narcissus tazetta* var. *chinensis* stimulated proliferation of mouse splenocytes and bone marrow cells but inhibited proliferation of leukemia L1210 cells. It also inhibited translation in a cell-free rabbit reticulocyte lysate system⁽⁶²⁾.

A methanol extract of the flowers of *Narcissus tazetta* var. *chinensis* possessed inhibitory effects on melanogenesis in theophylline-stimulated murine B16 melanoma 4A5 cells⁽⁵⁸⁾.

Antioxidant effects:

Antioxidant activity of *Narcissus tazetta* bulb was studied using DPPH and FRAP assay. Maximum inhibition of DPPH radical and IC₅₀ value were (99.89% and 2379.82±37.59 µg/ml respectively). In FRAP test, the antioxidant value was estimated as 0.29±0.02 mM/mg SO₄Fe⁽³³⁾.

Eleven compounds: tazetones C- G, (2S)-3',4'-dihydroxy-7-methoxyflavan, (2S)-3',7-dihydroxy-4'-methoxy-8-methylflavan, (2S)-liquiritigenin 7-methyl ether, 8-methylnaringenin, farrerol, and cyrtominetin, isolated from the bulbs of *Narcissus tazetta* var. *chinensis*, were evaluated for antioxidant effect against H₂O₂-induced impairment in human SH-SY5Y neuroblastoma cells by testing the cell viability (%). All the isolated compounds possessed potent antioxidant activity at concentration range (2.5 to 40 µM) with the viability from 45% to 80.2%, of which compound [(2S)-3',4'-dihydroxy-7-methoxyflavan] exhibited higher viability (%) than those of positive control (vitamin E) at the three concentrations of 10.0, 20.0, and 40.0 µM⁽⁷⁵⁾.

Dermatological effects:

IBR-DORMIN® *Narcissus tazetta* bulb extract, both alone and in combination with other inhibitory agents, including ubiquinones like coenzyme Q, were studied in the prevention or treatment of skin disorders and complications of disorders resulting from cell damage caused by an aging-related isoform of NADH oxidase (arNOX). These agents bound arNOX and inhibited the ability of arNOX to generate reactive oxygen species⁽⁷⁶⁾.

Neutral red assay was carried out to determine the proliferation effect of various concentrations of percolated extract of *Narcissus tazetta* on primary human dermal fibroblasts. 48 hr after cells treatment, the percolated extract didn't possess any significant effect (P>0.05) on the proliferation of fibroblast cells compared to untreated cells and IC₅₀= 35.19. The results of fibroblast migration showed that percolated extract increased cell migrations at low concentrations (1.562 and 3.125 µg/ml) while there was no migration at higher concentrations. Gap width decreased significantly at 1.562 and 3.125 µg/ml in comparison with untreated cells (P<0.01) (respectively 33.08% and 32.85%) after 24 hr. Furthermore, percolated extract caused significant decrease in gap width at 6.25 µg/ml (P<0.01) and 10 and 12.5 µg/ml (P<0.05) (38.08%, 26.65% and 23.69% reduction, respectively) after 48 hr in comparison to untreated cells⁽³³⁾.

Cardiovascular effects:

The aqueous (A) and 30% methanolic (B) fractions of an ethanol extract of the bulbs of *Narcissus tazetta* were studied for cardiovascular effects using *in vivo* and *in vitro* preparations of normotensive rats in the presence and absence of various (α , β -adrenergic, cholinergic, ganglionic, histaminergic, enzyme conversion inhibitor and calcium channel blockers). The fractions produced similar dose-dependent hypotensive responses in the anesthetized animals. The responses induced by fraction B might be mediated via adrenergic and cholinergic receptor activation. In isolated atrial preparations, fraction A possessed positive chronotropism without inotropic effect, while, fraction B produced negative chronotropic and positive inotropic effects⁽⁷⁷⁾.

Immunomodulatory effects:

The immune-modulation of *Narcissus tazetta* lectin on the induction of gene expression of cytokines in the mouse was studied, using specific cytokine primers, total RNA isolated from mouse splenocytes and macrophages, and reverse transcription-polymerase chain reaction. *Narcissus tazetta* lectin induced the expression of IL-1 β , TNF- α , and immune-reactive nitric oxide synthase in both splenocytes and macrophages *in vivo* after 10 day consecutive peritoneal injections of 5 mg *Narcissus tazetta* lectin /kg/day in the mouse. The expression levels of IFN- γ and TGF- β were markedly increased in macrophages, and the levels of IL-2 and IL-4 were up regulated only in splenocytes⁽⁷⁸⁾.

Other effects:

Three lectins were isolated from the bulbs of the Chinese daffodil *Narcissus tazetta*, they were differed in hemagglutinating activity, with the magnitude of the activity correlating with the ionic strength of the buffer required to elute the lectin from the DEAE-cellulose column. The bulb lectin did not exert potent cytotoxicity against cancer cell lines or fetal bovine lung cells but inhibited syncytium formation, and reinstated viability of, fetal bovine lung cells infected with bovine immunodeficiency virus⁽⁵³⁾.

Toxicity and side effects:

The American association of poison control centers received more than 47,000 reports of poisoning in 2011 due to toxic plant exposure. Of these, less than 1% were due to *Narcissus*. All parts of this plant were poisonous especially if large amounts were consumed. Patients may be asymptomatic or presented with nausea and severe vomiting, diarrhea, nervous symptoms such as trembling, and convulsions. Death can result from ingestion of the bulb. Irritant dermatitis can also occur when the needle-sharp calcium oxalate crystals, distributed in the outer layers of many *Narcissus* bulbs, pierce the hands of those handling them. The wheals are characteristic of the disorder suggested histamine release. Pre-hospital treatment included ceasing contact with the plant immediately and strict washing of hands, and eye irrigation in cases where patients rubbed their eyes with contaminated hands. Airway, breathing and circulation must be ensured, followed by supportive therapy including removal of any remaining toxin by gastric decontamination. Gastric lavage is unlikely to be effective. Gastrointestinal decontamination by activated charcoal may be beneficial by reducing the absorbed poison dose, only if administered within the first hour⁽⁷⁹⁾.

A purified protein (narcin, 13 kD) from the bulbs of *Narcissus tazetta* was characterized to be responsible for allergenic response. The protein was found to induce pro-inflammatory cytokines and thus induce allergy by elevating total IgE level⁽⁸⁰⁾.

III. CONCLUSION:

The current review discussed the traditional uses, bioactive ingredients, pharmacological and therapeutic importance of *Narcissus tazetta* as a promising medicinal plant with wide range of pharmacological activities which could be utilized in several medical applications.

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