Cynomorium plants: bioactive compounds and pharmacologic actions

Jiří Patočka 1,2 ORCID 0000-0002-1261-9703, Zdeňka Navrátilová 3 ORCID 0000-0001-5027-901X

1 Institute of Radiology, Toxicology and Civil Protection, Faculty of Health and Social Studies, University of South Bohemia in Ceske Budejovice, Ceske Budejovice, Czech Republic
2 Biomedical Research Centre, University Hospital, Hradec Kralove, Czech Republic
3 Department of Botany, Faculty of Science, Charles University in Prague, Czech Republic

Received 23rd November 2019. Accepted 9th January 2020. Published 5th June 2020.

Summary

Cynomorium coccineum and Cynomorium songaricum are unusual parasitic plants in the family Cynomoriaceae characterized by their unusual appearance and way of life. Due to their special habit and extremely rare occurrence, in the past, various magical properties have been attributed to these plants. The plant Cynomorium coccineum, which is found in the Mediterranean, has been used in Europe since the Middle Ages in folk medicine under the name fungus maletensis (maltese fungus). It was used for the same purpose in Arabic cultures under the name tarthuth. The Asian species (Cynomorium songaricum), sometimes considered a subspecies of C. coccineum, is still used in traditional Chinese medicine under the name Suo Yang. Recent studies show that the plant has a number of beneficial effects on the body and there is a real possibility that the substances present in Suo Yang or substances derived therefrom will be used in the future for therapeutic purposes. Of particular interest are their effects on sexual function. Preclinical experiments in male rats showed an increase in fertility after administration of Cynomorium extract. In these tests, an increase in the weight of the testes and an increase in the number of spermatozoa and their viability were observed. Cynomorium plants offer a new approach to the treatment of human infertility, which is currently a major problem.

Key words: Cynomorium; Maltese fungus; traditional medicine; man infertility

Introduction

The use of medicinal plants has accompanied mankind throughout its history. Fragments of some medicinal plants (Ephedra, Althaea, Achillea) were found even in the 60,000-year-old settlements of Neanderthals. Cannabis has been used in China 8,000 years ago and in Mesopotamia, poppy has been used at least 4,500 years ago. The Egyptian Ebers Papyrus, which dates back to 1,550 BC, lists a number of medicinal plants that were used at that time (Tyler, 2000; Samuelsson and Bohlin, 2010). Also nowadays, substances from plants and substances derived from them are of a great importance as medicines for many diseases. Some natural substances may be used directly, others serve as precursors for the production of other semi-synthetic bioactive substances. Also interesting is the possibility of using the known chemical structure of a natural substance as an inspiration in the development of new
drugs (Shu, 2005; Jones et al., 2006). Many plants have been given magical properties due to their special appearance. Plants that have been attributed an effect on sexual function have been of great interest. *Cynomorium* is one of these plants (Navratilova and Patocka, 2011; Lee et al., 2013; Gu et al., 2018).

**Botany**

The genus *Cynomorium* L. comprises two species of dicotyledonous parasitic plants with a unique appearance, according to which they were previously described as fungi. The genus was previously classified in the family *Balanophoraceae* (Tutin et al., 1964), but was later assigned to a special family of *Cynomoriaceae* based on morphological features and molecular data (Stevens, 2001). The family *Cynomoriaceae* comprises two species of the genus *Cynomorium* – *Cynomorium coccineum* L. (Fig. 1) and *Cynomorium songaricum* Rupr. (Heywood et al., 2007). *C. songaricum* is sometimes considered a subspecies of *C. coccineum* (Wu et al., 2007; Bellot et al., 2016). Plants are obligatory parasites because they lack chlorophyll. They consist of underground rhizomes with numerous haustoria, which attach to the host plant and draw nutrients from it. The leaves are reduced to scales. The host plants are usually halophytic species on the seashore (e.g. *Atriplex*, *Limonium*, *Tamarix*, *Salsola*, *Obione*, *Nitraria* and some species of the *Cistaceae* family). In spring and summer they grow on the surface of the inflorescence in the form of ears, 15–30 cm tall, consisting of small, densely crowded flowers of reddish-brown to purple-black color. Unlike the *Balanophoraceae* family, in addition to male and female flowers, there are two-flowered flowers in the inflorescence (Weber, Kendzior, 2006; Heywood et al., 2007). The flowers give off a sweet scent and are pollinated by flies (Lebling, 2003). *C. coccineum* grows rarely on rocky coasts in arid areas of Mediterranean and North Africa, *C. songaricum*, also known as Suo Yang, grows in the Middle East and extends to Central and West Asia. This plant is used in medicine, mainly for the treatment of premature ejaculation and impotence. The vast majority of scientific publications on *Cynomorium* plants are devoted to *C. songaricum*.

![Figure 1. Cynomorium coccineum (Photo: Michal Ducháček)](image)

**Ethnobotany**

*Cynomorium* plants have long been used for medicinal purposes. In Europe they were used in the Middle Ages under the name fungus maletensis (Maltese mushroom) according to a well-known site on a rocky cliff near the Maltese island of Gozo (Gebla tal-General, General's Rock, now Fungus Rock). The reef is poorly accessible, about 60 m high and 180 m long (Lebling, 2003) (Fig. 2). The rarity and mystical nature of the plant has led people
to attribute special power to it. Based on the signature theory, the plant was attributed to a phallic shape to help treat sexual problems. This property, together with its extraordinary rarity, made it highly valued (Attenborough, 1995). Knights of St. John of Jerusalem, they knew the plant already from Jerusalem. When they were forced to leave Jerusalem in the 16th century, they resorted to Malta and found *Cynomorium* on Fungus Rock. He was then closely guarded by soldiers and the thieves awaited severe punishment (sent to galleys and death). In 1651, the Dwejra Tower was built to protect the reef with its growing *Cynomorium*. Knights Hospitaller used dried inflorescences to stop bleeding, prevent infections and to regenerate after combat (Leonti et al., 2020). The plant was also used to treat stomach problems, dysenteria, diarrhoea, hemorrhoids and as an aphrodisiac. Dried inflorescences were sent as a valuable gift to European kings, queens and nobility (Attenborough, 1995; Lebling, 2003; Patočka et al., 2010). Carl von Linné (1755) also mentions the plant. The plant also played a very important role in Arab countries, where it was used under the name *tarthuth*, for example, to treat high pressure, vomiting, colic, stomach ulcers, irregular menstruation, impotence, infertility and venereal diseases. In addition, *Cynomorium* has been used for food, as a spice and as a fabric coloring agent (Lebling, 2003; Nickrent et al., 2005; Heide-Jørgensen, 2008). *C. songaricum* had an important position in traditional Chinese medicine. Under the name *Suo Yang*, it has been used as a tonic and for the treatment of kidney diseases, digestion and impotence (Lebling, 2003; Nickrent et al., 2005; Wu et al., 2007). For medical reasons the interest in recent years seems to have increased again, and measures must be taken to protect it (Heide-Jørgensen, 2008).

**Bioactive substances**

*C. coccineum* and *C. songaricum* contain many bioactive compounds (Rosa et al., 2012; Zucca et al., 2016; Sdiri et al., 2018). More than 30 compounds including 8 triterpenoids, 6 flavonoids, 8 phenolic acids, 4 fatty acids, and others have been detected and identified in *Cynomorium coccineum* (Li et al., 2020). A similar situation was also found in *Cynomorium songaricum* (Cui et al., 2019).

The pharmacologically most important can be considered.

**Triterpenoids**

Ursolic acid, acetylursolic acid, malonylursolic acid hemiester, ursonazole-12-ene-28-acid-3β malonic acid monoester, oleanolic acid, betulinic acid and triterpenoid saponins have been isolated from *Cynomorium* (Ma et al., 1999; Ma et al., 2009). Triterpenoids of *Cynomorium* could be perspective drugs for treating of cancer (Cheng et al., 2017).
Flavonoids

Many flavonoids are known to have a number of biological activities such as antioxidant, antiinflammatory, antibacterial, antifungal, antiviral and anticancer functions. The main flavonoids in Cynomorium are (+)-catechin and (-)-catechin (Hiroki, 1989; Chu et al., 2006; Yu et al., 2010), epicatechin (Tao et al., 1999), (-)-epicatechin-3-O-gallate (Xie et al., 2016), proanthocyanidins (Zhang et al., 2007), citrusin-4-O-glucopyranoside (Cheng et al., 2017), glycosides of citrinin (Qu et al., 2016), epicatechin gallate (Chen and Hatano, 2007) and epiphyllocoumarin (Wang et al., 2015). Other important flavonoids are rutin, quercetin, isoquercetin, isoquercitrin, naringenin, luteolin and phloridzin (Cui et al., 2013; Wang et al., 2015).

Steroids

Cynomorium contains a number of steroids such as β-sitosterol and daucosterol or β-sitosterol oleate (Ma et al., 1993), β-sitosterol palmitate (Chaomei et al., 1999), β-sitosterol-β-D-glucoside (Ma et al., 2002), 5α-stigmasterol-9 and its esters (Qu et al., 1991). Steroids are important bioactive compounds and also play an important role in the pharmacological action of these plants (Xu et al., 1996).

Saccharides, Polysaccharides and other Sugar Derivatives

Glucose (Tao et al., 1999), sucrose (Zhang and Zhang, 1991), ginger oil ketones glucoside (Chaomei et al., 1999), polysaccharides (Zhang and Xue, 1995; Lv et al., 2000) and heteropolysaccharides (Zhang et al., 2001), n-butyl-α-D-fructofuranoside and n-butyl-β-D-fructofuranoside (Sheng et al., 2000; Zhang et al., 2002) were found in Cynomorium plants.

Other Substances

From the pharmacologically less important substances, severe proteinogenic and non-proteinogenic amino acids (Fu et al., 1997; Lin et al., 2000), carboxylic acids (Hiroki, 1989; Chen and Hatan, 2007; Qu et al., 2016; Xu et al., 1996; Tao et al., 1999), phenylpropanoids (Cui et al., 2013), lignins (Jiang et al., 2001; Wang and al., 2015), essential oil (Zhou et al., 2009), and condensed tannins (Zhang et al., 1991; Lin et al., 2000; Chang et al., 2005; Zhang et al., 2005) were found in Cynomorium. However, as Ben Attia and coworkers (2018) have shown, the chemical composition and antioxidant effects and biological activity of Cynomorium coccineum grown at different sites can vary significantly. Similar situation was found in composition od bioactive substances of Cynomorium songaricum. (Cui et al., 2019). In the seven main production areas of China, differences in the chemical composition of bioactive compounds were found and the study revealed that one of the possible factors that may influence the composition of plant secondary metabolites is endophytic fungi (Cui et al., 2019).

Bioactivity

The bioactive substances of Cynomorium plants have a number of effects on the body (Meng et al., 2013). Recent studies confirm some empirically acquired knowledge of the use of plants in the past. C. songaricum have promising effects against inflammation, aging, fatigue, viruses and cancer and protective effect on the nervous system. This plant also have antifungal effect (Gonçalves et al., 2015), regulates hormones and immune functions (Wang et al., 2016) and also exhibits a neuroprotective and antidepressant effect and improves cognitive functions (Cheng et al., 2017; Miao et al., 2017).

Extract of fresh C. coccineum plant has a hypotensive effect, the active ingredient has not been identified (Ikram et al., 1978). In vitro, C. coccineum extract has an antioxidant potential (Zucca et al., 2013), antiproliferative effects on human cancer lines and antiviral activity against a panel of mammalian viruses (Rosa et al., 2015; Vascellari et al., 2019). In vivo, C. coccineum treatment prolonged a survival of mice with cancer (Sdiri et al., 2018). Flavonoids have an antioxidant effect and act against fatigue. Experimentally, an increase in the performance of rats in the buoyancy test after administration of C. songaricum was confirmed (Yu et al., 2009; 2010). C. songaricum ingredients also have an antiviral effect, acting as HIV-1 protease inhibitors (Ma et al., 1999; Nakamura, 2004). In vitro, the function of neurotransmitter transporters (GAT-1, DAT, NET, SERT) was affected. C. songaricum
extract acts as a DAT/NES activator and GAT-1/SERT inhibitor; increases the dopamine and noradrenaline uptake and decreases the GABA and serotonin uptake (Zhao et al., 2010).

Orally administered *Cynomorium songaricum* extract to ovariectomized rats had a learning and memory enhancing effect in the Morris water maze assay and its effect was probably exerted by p-CREB / BDNF mediated ERK / p38MAPK regulative (Tian et al., 2019). *In vitro*, *Cynomorium songaricum* extracts protect human neuroblastoma cells from β-amyloid and superoxide anion induced injury (Lu et al., 2009). They also prevent damage to nerve and muscle cells during hypoxia, increase superoxide dismutase activity and reduce malonylaldehyde and lactic acid content in nervous cells. They also affect the protein content of muscle cells (Luo et al., 2007). The extract also improves the learning process and memory (Zhao et al., 2002). In perimenopausal rats, *Cynomorium* flavonoids attenuate depressive symptoms (Miao et al., 2017). *C. songaricum* ingredients enhance humoral and nonspecific immunity in mice after cyclophosphamide immunusuppression (Zhang et al., 2008). Very interesting are the effects on the genital system. *Cynomorium songaricum* extract enhances spermatogenesis and expression of GDNF (a factor secreted by Sertoli cells that induces proliferation of undifferentiated spermatogonia). In an experiment in rats, an increase in sperm count and testicular weight was observed when administering the extract (Yang et al., 2010). In another experiment, similar results were obtained after administration of *C. coccineum* and *Withania somnifera* (Abdel-Magied et al., 2001). *Cynomorium coccineum* extract strengthened the spermatogenesis also in golden hamsters (Lee et al., 2013). Gonadotropin levels and ovarian weight changes were altered in females (Al-Qarawi et al., 2000). The administration of *C. coccineum* extract resulted in an increase in male sperm count and an increase in the proportion of living sperms and their motility (Abdel-Rahman et al., 1999).

A randomized, double-blind, placebo-controlled crossover study of Cappra® for the treatment of mild or mild to moderate erectile dysfunction in Thai male was provided. Cappra® is a herbal medicine which consists of 13 Chinese herbs including *Cynomorium songaricum*. The efficacy was assessed by the International Index of Erectile Function (IIEF) questionnaire and adverse events. There was an improvement of IIEF score for all domains in Cappra® group compared with placebo group. The mean change of IIEF score from baseline for erectile function domain of Cappra® was significantly higher than placebo (4.87 vs. 3.44, p = 0.032) (Punyawudho et al., 2012).

A major problem for many developed countries is the steady decline in birth rates, which is due to a number of factors. An important cause is the rise of male infertility, the main cause of which is the inability to produce enough healthy sperm (Krausz, 2011). *Cynomorium* resp. the ingredients of this plant, with their positive effect on spermatogenesis, present a challenge for contemporary medicine, which is not yet very successful in the treatment of male infertility.

**Toxicity**

Acute toxicity, genetic toxicity and the 90-day repeated oral toxicity of *C. songaricum* (Suo Yang) have been studied in mice (Wei et al., 2019). The acute toxicity test revealed no unusual behavior or increased animal mortality. It has been found that the maximum tolerable dose of this herbal preparation is greater than 15 g/kg. No toxicity effects were observed in three genotoxicity studies. For genotoxicity testing, a bacterial reverse mutation assay, a mouse micronucleus bone marrow assay and a chromosomal spermatocyte aberration assay were used. No increased micronucleus frequencies or structural abnormalities of spermatocyte chromosomes were found in *in vivo* assays. In a 90-day subchronic oral toxicity study in Wistar rats, no haematological changes were observed, nor were any significant toxicological manifestations in the clinical investigation. The NOAEL was 2.83 g/kg of body weight and LOAEL was 5.66 g/kg of body weight (Fu et al., 2019). All of these results suggest that Suo Yang at a given dose is a safe herbal remedy.

**Perspectives and Conclusions**

Scientific research into new safe and effective drugs has recently rediscovered natural substances as a huge reservoir of innovative therapeutic agents for human health. Relatively recently, several research groups have begun to seek confirmation of the effect of some traditional treatments with natural substances and to study their previously unknown biological activities (Zucca et al., 2019). Recent animal studies show that the substances of *C. coccineum* and *C. songaricum* have a number of interesting effects on the body. Numerous studies have confirmed the empirical...
knowledge gained over thousands of years of use of these plants. Further research is therefore perspective and their use in the future can be expected. Abroad, dietary supplements containing plant extracts for the treatment of sexual dysfunctions are on the market. It is not clear how many active substances these preparations contain (if any). Experiments Griffin et al. (2017) provided initial evidence for the direct production of high-quality *Cynomorium* nanoparticles with preserved biological activity. This may be more convenient and much cheaper for the preparation of medicaments than the time-consuming extraction, separation and isolation of individual biologically active compounds. What is certain, however, is the need to develop cultivation techniques for the cultivation of these plants. The cultivation of parasitic plants is problematic, but their excessive collection in the wild threatens to eventually kill of them (Nickrent et al., 2005). Once an extinct species is lost forever (evolution does not repeat), it is important to preserve not only these species for the future.

**Funding**

This work was supported from Institutional support for a long-term conceptual project of the University Hospital Hradec Králové, Czech Republic. The authors thank Mgr. Michal Duchacek and Mgr. Elena Rimekova for unique photos.

**Conflict of Interest**

The authors declare that there is no conflict of interest with regard to the topic, creation and publication of this article, and no pharmaceutical company has supported the creation or publication of the article.

**Adherence to Ethical Standards**

This article does not contain any studies involving animals performed by any of the authors.

This article does not contain any studies involving human participants performed by any of the authors.

**References**

1. Abdel-Magied EM, Abdel-Rahman HA, Harraz FM. The effect of aqueous extracts of *Cynomorium coccineum* and *Withania somnifera* on testicular development in immature Wistar rats. J Ethnopharmacol. 2001;75(1):1–4.
2. Abdel-Rahman HA, el-Badry AA, Mahmoud OM, Harraz FA. The effect of the aqueous extract of *Cynomorium coccineum* on the epididymal sperm pattern of the rat. Phytother Res. 1999;13(3):248–250.
3. Al-Qarawi AA, Abdel-Rahman HA, El-Badry AA, Harraz F, Razig NA, Abdel-Magied EM. The effect of extracts of *Cynomorium coccineum* and *Withania somnifera* on gonadotrophins and ovarian follicles of immature Wistar rats. Phytother Res. 2000;14(4):288–290.
4. Attenborough D. *The Private Life of Plants*. Princeton University Press. 1995; 320 p.
5. Bellot S, Cusimano N, Luo S, Sun G, Zarre S, Gröger A, Temsch E, Renner SS. Assembled plastid and mitochondrial genomes, as well as nuclear genes, place the parasite family Cynomoriaceae in the Saxifragales Genome Biol Evol Open Access, 2016;8(7):2214–2230.
6. Ben Attia I, Zucca P, Cesare Marincola F, Piras A, Rosa A, Chaieb M, Rescigno A. Chemical composition and antioxidant potential differences between *Cynomorium coccineum* L. growing in Italy and in Tunisia: Effect of environmental stress. Diversity, 2018;10(3):53.
7. Chang Y, Su G, Yin C, Zhang J, Bu H. Study on Dynamics of Tannin in different Growth Phase of *Cynomorium songaricum*. J Chin Med Mater. 2005;28:643–645.
8. Chaomei MA, Nakamura N, Miyashiro H, Hattori M, Shimotohno K. Inhibitory effects of constituents from *Cynomorium songaricum* and related triterpene derivatives on HIV-1 protease. Chem Pharm Bull. 1999;47:141–145.
9. Chen G, Hatano T. Studies on chemical constituents in stems of *Cynomorium songaricum* Rupr. J Xinjiang Univ. 2007;24:87–91.
10. Cheng D, Zheng J, Ma S, Murtaza G, Wahab A, Yu C, Liu J, Lu Y. Chemical constituents, and pharmacological and toxicological effects of *Cynomorium songaricum*: An overview. Tropical J Pharmaceut Res. 2017;16(11):2689–2696.
11. Chu Q, Tian X, Li M, Ye J (2006). Electromigration profiles of *Cynomorium songaricum* based on capillary electrophoresis with amperometric detection. J Agric Food Chem. 2006;54(21):7979–7983.
12. Cui JL, Gong Y, Vijayakumar V, Zhang G, Wang ML, Wang JH, Xue XZ. Correlation in chemical metabolome and endophytic mycobiome in Cynomorium songaricum from different desert locations in China. J Agr Food Chem. 2019;67(13):3554–3564.

13. Cui Z, Guo Z, Miao J, Wang Z, Li Q, Chai X, Li M. The genus Cynomorium in China: an ethnopharmacological and phytochemical review. J Ethnopharmacol. 2013;147(1):1–15.

14. Fu B, Qiao J, Du N. Analysis of trace elements and amino acids in Chinese medicine Cynomorium. J Xinjiang Med Coll. 1997;20:127–128.

15. Fu S, Xu S, Pei D, Qu W, Qu J, Tian J. [Subchronic toxicity test of songaria cynomorium herb aqueous extract in rat]. Wei Sheng Yan Jiu. 2019;48(1):104–108. Article in Chinese.

16. Gonçalves MJ, Piras A, Porcedda S, Morongiu B, Danilo F, Cavaleiro C, Rescigno A, Rosa A, Salgueiro L. Antifungal activity of extracts from Cynomorium coccineum growing wild in Sardinia island (Italy). Nat Prod Res. 2015;29(23):2247–2250.

17. Griffin S, Alkhayer R, Mirzoyan S, Turabyan A, Zucca P, Sarfraz M, Nasim MJ, Trchounian A, Rescigno A, Keck CM, Jakuba C. Nanosizing cynomorium: Thumbs up for potential antifungal applications. Inventions, 2017;2(3):24.

18. Gu S, Zhou R, Wang X. Comparison of enhanced male mice sexual function among three medicinal materials. Andrologia. 2018;50(9):e13087.

19. Heide-Jørgensen H. Parasitic Flowering Plants. Brill Academic Publishing. 2008; 438 p.

20. Heywood VH, Brummit RK, Culham A, Seberg O. Flowering Plant Families of the World. Firefly Books, Ontario. 2007; 424 p.

21. Hiroki S. Composition of Kampo Complement (1)-the Ingredients of Cynomorium. Foreign Med Sci – Section Tradit Chin Med. 1989;11:36–42.

22. Ikram M, Alkhayer R, Mirzoyan S, Turabyan A, Zucca P, Sarfraz M, Nasim MJ, Trchounian A, Rescigno A, Keck CM, Jakuba C. Hypotensive agent from Cynomorium coccineum. Pahlavi Med J. 1997;9(2):167–181.

23. Jiang ZH, Tanaka T, Sakamoto M, Jiang T, Kouno I. Studies on a medicinal parasitic plant: lignans from the stems of Cynomorium songaricum. Chem Pharm Bull (Tokyo). 2001;49(8):1036–1038.

24. Jones WP, Chin Y-W, Kinghorn AD. The role of pharmacognosy in modern medicine and pharmacy. Curr Drug Targets, 2006;7(3):247–264.

25. Krausz C. Male infertility: pathogenesis and clinical diagnosis. Best Pract Res Clin Endocrinol Metab. 2011;25(2):271–285.

26. Lebling RV. The Treasure of Tarthuth. Saudi Aramco World. 2003;54:12–17.

27. Lee JS, Oh HA, Kwon JY, Jeong MH, Lee JS, Kang DW, Choi D. The Effects of Cynomorium songaricum on the Reproductive Activity in Male Golden Hamsters. Dev Reprod. 2013;17(1):37–43.

28. Leonti M, Bellot S, Zucca P, Rescigno A. Astringent drugs for bleedings and diarrhoea: The history of Cynomorium coccineum (Maltese Mushroom). J Ethnopharmacol. 2020;249:112368.

29. Lin Y, Liu B, Chen J. Study on Chemical Constituents of Cultivated and Wide Cynomorium. J Med Pharm Chin Minorities. 2000;6:60–61.

30. Li X, Sdiri M, Peng J, Xie Y, Yang BB. Identification and characterization of chemical components in the bioactive fractions of Cynomorium coccineum that possess anticaner activity. Int J Biol Sci. 2020;16(1):61–73.

31. Lu Y, Wang Q, Melzig MF, Jenett-Siems K. Extracts of Cynomorium songaricum protect human neuroblastoma cells from beta-amyloid 25-35 and superoxide anion induced injury. Pharmazie. 2009;64(9):609–612.

32. Luo JD, Zhang RX, Jia ZP, Li M, Wang J, Hu J. Pharmacological effects and mechanism of anti-hypoxia components from Cynomorium songaricum Rupr. Tradit Chin Drug Res Clin Pharmacol. 2007;18:275–279.

33. Lv Y, Gao F, Yu T, Tian X. Determination of the polysaccharide of Cynomorium songaricum. J Med Pharm Chin Minorities. 2000;12:63–65.

34. Ma C, Jia S, Sun T, Zhang Y. Triterpenes and steroidal compounds from Cynomorium songaricum. Acta Pharm Sinica. 1993;28:152–155.

35. Ma CM, Wei Y, Wang ZG, Hattori M. Triterpenes from Cynomorium songaricum – analysis of HCV protease inhibitory activity, quantification, and content change under the influence of heating. J Nat Med. 2009;63(1):9–14.

36. Ma C, Nakamura N, Hattori M, Cai S. Isolation of malonyl oleanolic acid hemiester as anti-HIV protease substance from the stems of Cynomorium songaricum. Chin Pharm J. 2002;37:336–338.

37. Ma C, Nakamura N, Miyashiro H, Hattori M, Shimotohno K. Inhibitory effects of constituents from Cynomorium songaricum and related triterpene derivatives on HIV-1 protease. Chem Pharm Bull (Tokyo). 1999;47(2):141–145.
38. Meng HC, Wang S, Li Y, Kuang YY, Ma CM. Chemical constituents and pharmacologic actions of Cynomorium plants. Chin J Nat Med. 2013;11(4):321–329.
39. Miao M, Yan X, Guo L, Li P. Effect of Cynomorium total flavone on depression model of perimenopausal rat. Saudi J Biol Sci. 2017;24(1):139–148.
40. Navratilová Z, Patocka J. [Cynomorium – bizar plant with medical potential]. Pevence úrazů, otrav a násilí 2011;7(2):199–203. Article in Czech.
41. Nickrent DL, Der JP, Anderson FE. Discovery of the photosynthetic relatives of the „Maltese mushroom“ Cynomorium. BMC Evol Biol. 2005;5:38.
42. Patocka J, Jakl J, Rimekova E. Tajemství maltské „houby“. Vesmír. 2010;89(6):348.
43. Punyawudho B, Puttilerpong C, Wirotsaengthong S, Aramwit P. A randomized, double-blind, placebo-controlled crossover study of Cappra® for the treatment of mild or mild to moderate erectile dysfunction in Thai male. Afr J Tradit Complement Altern Med. 2012;10(2):310–315.
44. Qu L, Yin X, Fan S, Qian Y. Genetic Toxicity of Cynomorium Songaricum. J Med Pest Control. 2016;32:275–278.
45. Qu S, Wu H, Hu S. A Preliminary Study on the Chemical Constituents of Cynomorium songaricum. Acta Acad Med Xinjiang. 1991;14:207–208.
46. Rosa A, Nieddu M, Piras A, Atzéri A, Putzu D, Rescigno A. Maltese mushroom (Cynomorium coccinum L.) as source of oil with potential anticancer activity. Nutrients, 2015;7(2):849–864.
47. Shu YZ. Natural products drug discovery – success, challenge and developability perspective. J Trad Med. 2005;22(Suppl. 1):104–115.
48. Stevens, P. F. (2001 onwards). Angiosperm Phylogeny Website. Version 14, July 2017. http://www.mobot.org/MOBOT/research/APweb/.
49. Vascellari S, Zucca P, Perra D, Serra A, Piras A, Rescigno A. Antiproliferative and antiviral activity of methanolic extracts from Sardinian Maltese Mushroom (Cynomorium coccinum L.). Nat Prod Res. 2019:1–5.
50. von Linné C. Dissertatio botanico-medica in qua Fungus melitensis com Consens. Experient Facult Med Almo Upsal Lyceae – Praeside viro nobilissimo Carolo Linnaeo. Höjer LM, 1755.
51. Wang F, Liu Q, Wang W, Li X, Zhang J. A polysaccharide isolated from Cynomorium songaricum Rupr. protects PC12 cells against H2O2-induced injury. Int J Biol Macromol. 2016;87:222–228.
52. Wang X, Li H, Liu M, Jiao H. Chemical constituents from Cynomorium songaricum Rupr. Chin Tradit Pat Med. 2015;37:1737–1739.
53. Weber HC, Kendzior B. Flora of the Maltese Islands – A Field Guide. Margraf Publishers Germany. 2006;384 p.
54. Wei F, He Q, Wang W, Pei D, Zhang B. Toxicity assessment of Chinese herbal medicine Cynomorium songaricum Rupr. Evid Based Complement Alternat Med. 2019;2019:9819643.
55. Wu Z, Raven PH, Deyuan H (eds.). Flora of China. Vol. 13. Clusiaceae through Araliaceae. Missouri Botanical Garden Press. 2007; 548 p.
56. Xie S, Li G, Zhang K, Wang H, Tan Y, Wang J. Isolation and identification of chemical constituents from Cynomorium songaricum. J Shenyang Pharm Univ. 2012;29:525–528.
65. Xu X, Zhang C, Li C. Chemical components of Cynomorium songaricum Rupr. Zhongguo Zhong Yao Za Zhi. 1996;21(11):676–677,704.
66. Yang WM, Kim HY, Park SY, Kim HM, Chang MS, Park SK. Cynomorium songaricum induces spermatogenesis with glial cell-derived neurotrophic factor (GDNF) enhancement in rat testes. J Ethnopharmacol. 2010;128(3):693–696.
67. Yu FR, Feng ST, Xie MR, Lian XZ. Anti-fatigue effect of Cynomorium songaricum flavone on old rats. Chin J Rehab Theory Pract. 2009;14:1141–1142.
68. Yu FR, Liu Y, Cui YZ, Chan EQ, Xie MR, McGuire PP, Yu FH. Effects of a flavonoid extract from Cynomorium songaricum on the swimming endurance of rats. Am J Chin Med. 2010;31(1):65–73.
69. Zhang B, Xiang Y, Zhou Q. Research status and development of Cynomorium songaricum Rupr. Liquor Making. 2002;29:72–73.
70. Zhang B, Zhang R, Lu X. Analysis and Determination of Tannin Type in Cynomorium songaricum. J Chin Med Mater. 1991;14:36–38.
71. Zhang CZ, Wang SX, Zhang Y, Chen JP, Liang XM. In vitro estrogenic activities of Chinese medicinal plants traditionally used for the management of menopausal symptoms. J Ethnopharmacol. 2005;98(3):295–300.
72. Zhang M, Xue D. Determination of Saccharides in Cistanehe Salsa and Cynomorium Songaricum. J Jiangxi Coll Tradit Chin Med. 1995;7:24–25.
73. Zhang RX, Jia ZP, Li MX, Wang J, Yin Q, Luo JD, Liu HY. Study on the effect of Part III from Cynomorium songaricum on immunosuppressive mice induced by cyclophosphamide. Zhong Yao Cai. 2006;31(3):407–409.
74. Zhang SJ, Zhang SY, Hu JP. Studies on polysaccharide of Cynomorium songaricum Rupr. Zhongguo Zhong Yao Za Zhi. 2001;26(6):409–411.
75. Zhang S, Wang Y, Liu L, Yu J, Hu J. Studies on Chemical constituents of Herba cynomorium II. Chin Pharm J. 2007;42:975–977.
76. Zhang S, Zhang S. Chemical constituents of Cynomorium songaricum. Chin Pharm J. 1991;26:649–651.
77. Zhang S, Zhang S, Hu J. Studies on Polysaccharide of Cynomorium songaricum Rupr. Chin J Chin Mater Med. 2001;26:409–411.
78. Zhao G, Wang J, Qin GW, Guo LH. Cynomorium songaricum extracts functionally modulate transporters of gamma-aminobutyric acid and monoamine. Neurochem Res. 2010;35(4):666–676.
79. Zhao YQ, Wang ZW, Jing YH. The study on the effect of Suoyang on ultrastructural in the relevant brain areas of learning and memory in the rat’s model of Alzheimer’s disease. Chin J Clin Rehabil. 2002;6:2220–2221.
80. Zhou YB, Ye RR, Lu XF, Lin PC, Yang SB, Yue PP, Zhang CX, Peng M. GC-MS analysis of liposoluble constituents from the stems of Cynomorium songaricum. J Pharm Biomed Anal. 2009;49(4):1097–1100.
81. Zucca P, Argiolas A, Nieddu M, Pintus M, Rosa A, Samna F, Sollai F, Steri D, Rescigno A. Biological Activities and Nutraceutical Potentials of Water Extracts from Different Parts of Cynomorium Coccinelleum L. (Maltese Mushroom). Polish J Food Nutr Sci. 2016;66 (3):179–188.
82. Zucca P, Bellot S, Rescigno A. The Modern Use of an Ancient Plant: Exploring the Antioxidant and Nutraceutical Potential of the Maltese Mushroom (Cynomorium coccinellum L.). Antioxidants (Basel). 2019;8(8).pii:E289.
83. Zucca P, Rosa A, Tuberoso CIG, Piras A, Rinaldi AC, Sanjust E, Dessi MA, Rescigno A. Evaluation of antioxidant potential of "Maltese mushroom" (Cynomorium coccinellum) by means of multiple chemical and biological assai. Nutrients. 2013;5(1):149–161.