WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 4, 154-169. Research Article ISSN 2277– 7105

MORPHO-ANATOMICAL FEATURES AND ANTIOXIDANT POTENTIAL OF BROUSSONETIA PAPYRIFERA (L.) VENT.

Vasilica Luchian*[1], Mariana Toma[1,2] and Aurora Dobrin[3]

[1]University of Agronomic Sciences and Veterinary Medicine of Bucharest, 59 Marasti Avenue, District 1, Bucharest, Romania.

[2]Institute of Research - Development for Processing and Marketing of Horticultural Products - "Horting", 5N Drumul Gilaului, District 4, Bucharest, Romania.

[3]Research Center for Studies of Food Quality and Agricultural Products, USAMV Bucharest, 59 Marasti Avenue, District 1, Bucharest, Romania.

Article Received on
08 Feb. 2021,
Revised on 01 March 2021,
Accepted on 22 March 2021
DOI: 10.20959/wjpr20214-20167

***Corresponding Author**
Vasilica Luchian
University of Agronomic Sciences and Veterinary Medicine of Bucharest, 59 Marasti Avenue, District 1, Bucharest, Romania.

ABSTRACT

Broussonetia papyrifera (syn. *Papyrius papyrifera* L. /Kuntze., *Morus papyrifera L.*), also known as paper mulberry is a medicinal plant, small tree or shrub which grows naturally in Asian and Pacific countries and in the southern part of USA. It has been successfully cultivated in some European countries, such as Italy, Slovenia, Ukraine, Hungary, Slovakia, Spain, etc. The analysed species has been cultivated for over 40 years at the Botanical Garden of the University of Agronomic Sciences and Veterinary Medicine of Bucharest. Various studies on the leaf morphology and stem, leaf and petiole anatomy have been carried out. The morphological analyses have showed that the leaves varied in length between 7-12 cm and in width between 5-7.5 cm. The petiole length was between 2-5 cm. The leaves of *B. papyrifera* presents adaxial and abaxial epidermis, cuticle and bifacial mesophyll. Biochemical analyses (total phenolic content, flavonoids and scavenging activity) on fresh leaves and fruits showed that leaves had the higher total polyphenols and flavonoids content than fruits, instead fruits exhibited a higher 2,2-diphenyl-2-picrylhydrazyl hydrate (DPPH) radical, hydroxyl radical scavenging activity than leaves.

KEYWORDS: paper mulberry, leaf & stem anatomy, antioxidants, Covid-19.

INTRODUCTION

Broussonetia papyrifera (genus: *Broussonetia*, family: *Moraceae*) also known as paper mulberry is a dioecious, deciduous tree or shrub native to Japan, China and Polynesia, which grows naturally in the Asian and Pacific regions.[1] Genus name honours Pierre Auguste Marie Broussonet (1761-1807), French physician, naturalist and one-time professor of botany at Le Jardin des Plantes de Montpellier.[2] The roots, leaves, bark and fruits of paper mulberry are all used in the traditional medicines.

The current Covid -19 pandemic is caused by the SARS CoV-2 virus. On March 11, 2020, the World Health Organization announced that the spread of the new coronavirus had reached the stage of a pandemic and to date (October 2020), there are more than 40 million confirmed cases in the world; at the same time, there is not yet an effective treatment for the disease.[3] Several attempts have been made in search of the effective drugs to control the spread of the SARS CoV-2 infection. It was already reported that the polyphenols of *Broussonetia papyrifera* inhibit efficiently the catalytic activity of SARS COV-1 and MERS Mpro. But whether these polyphenols exhibit any inhibitory effect on SARS CoV-2 Mpro is far from clear. Polyphenols having glucosidase inhibitory properties are reported to show antiviral activity against various coronaviruses, such as SARS CoV-1 and the A group of polyphenols from *Broussonetia papyrifera* are known to possess α-glucosidase inhibition activity.[4-8] Several other authors noted that a great deal of potentially valuable aromatic herbs and phytochemicals are awaiting assessment and exploitation for therapeutic use against genetically and functionally different virus families, including coronaviruses.[9-11] After the outbreak of SARS CoV, first described in 2003[12], different researchers and scientists have tried their best to explore various antiviral extracts, drugs and molecules against SARS-CoV.[13-23] *Broussonetia papyrifera* is used in the traditional medicine to treat different diseases, having anti-inflammatory effect, antioxidant capacity - being helpful even for pancreatic cancer.[24-26] Herbal remedies, such as the plant extracts or the phyto-constituents from certain parts and organs of the plant (e.g. root, stem, bark, seed, flower) are used as nutraceutic and nutritional supplements, as well, for treating various diseases.[27] A WHO report showed that 80% of the people living in developing nations depend on traditional plants for health requirements.[28] In the traditional medicine practiced in Indo - China, the leaves of *Broussonetia papyrifera* are used as a laxative and a diaphoretic, while the fruit as pectoral, stomachic and tonic; at the same time, the bark is taken against dysentery and haemorrhage. The latex is applied externally to treat snake and dog bites, as well as bee

stings. The root bark is used for skin depigmentation. The stem bark is diuretic and haemostatic.[29] A flavonoid, namely *broussochalcone A*, isolated from the bark, is a powerful antioxidant and has free radical-scavenging activity.[30]

It also suppresses the production of nitric oxide and, hence, it may have potential to cure various inflammatory diseases. *Broussonin* A and B from the bark have shown antifungal and antibacterial activity.[31] The chemical constituents of *B. papyrifera* have antiplatelet properties in humans.[30,31] Numerous studies have been conducted to reveal the medicinal properties of the species.[32-39] It has also been investigated for its properties as a pesticide.[40] The leaf powder, when fed to the cotton bollworm (*Helicoverpa armigers*) caused restriction in its pupation and adult emergence. The xylem contains an antifungal substance against *Fusarium* spp.[41] The Chinese herbals used to treat Covid -19 mainly included glycyrrhiza (*Glycyrrhiza glabra*), ephedra (*Ephedra sinica*), bitter almond (*Prunus dulcis* var. *amara*), gypsum, reed root (*Phragmites communis*), *Amomum sp.* and *Trichosanthe sp.* (*Cucurbitaceae*). Their main function is to relieve cough and to improve immunity.[23] At the same time, the plants of *Camellia sinensis L.*, having antiviral properties are effective SARS CoV-2, Mpro inhibitors.[42,43] It has been reported that China has widely used traditional Chinese aromatic herbs and medicinal plants for the successful treatment of SARS in several cases.[44] It has been known for almost 1,500 years as a plant whose bark can be used to make paper of various qualities up to the highest. The inner bark (bast vessels) is used for *tapa* (cloth) in the South Sea islands, while in Japan, Thailand, Myanmar, Indonesia it is used for special paper making, such as paper napkins, lens paper, cosmetic tissue and luxurious hand-made paper.[45] Based on the good economic potentiality and environmental effects, *Broussonetia papyrifera* is an important candidate for phytoremediation.[46]

MATERIALS AND METHODS

The material, *Broussonetia papyrifera* (female plant) originated from the Botanical Garden of the University of Agronomical Sciences and Veterinary Medicine of Bucharest, Romania.

This species adapted well here, having been cultivated for the past four decades. It showed immunity to various pests. A specimen of *B. papyrifera* was deposited at the Herbarium of the University of Agronomic Sciences and Veterinary Medicine of Bucharest, with the botanical voucher no. 4968.

The material was sectioned by hand using razor blades to obtain semipermanent and permanent slides for microscopic studies. Fresh leaves, stems and petioles were collected for anatomical study. Thereafter, the sections were clarified with chloral hydrate for 24 hours, then washed and stained with carmine alaunate and green iodine.[47] Analyses and observations of the cross-sections were performed at the Center for the Study of Food and Agricultural Products Quality at the University of Agronomic Sciences and Veterinary Medicine of Bucharest. Photos were taken and measurements were made using Leica DM1000 LED, Leica DFC295 Video Camera and Leica S8 APO Stereo Microscope, Novex Holland, Optika Microscope, as well as Sony photo camera. Photos were taken using a light microscope with different magnifications. The physicochemical analyses were carried out at the laboratories of the Research Center for Studies of Food and Agricultural Products Quality, University of Agronomic Sciences and Veterinary Medicine of Bucharest.

The extracts were prepared using 50% (v/v) ethanol, after the pharmacopoeia method. The total phenolic content was determined through the method of Dobrin et al.[48], using the Folin-Ciocalteu reagent and expressed as gallic acid equivalents per gram of fresh material (mg GAE/g FW).

The calibration curve of the gallic acid had the following concentrations: 0, 5, 10, 20, 30, 40, 50, 60, 70 and 80µg/ml. The $AlCl_3$ modified assay after Dobrin et al.[48] was used for the quantification of the total flavonoid content of the ethanolic plant extracts. Standard solutions of catechin for calibration curve were 0, 0.01, 0.05, 0.10, 0.20, 0.30 and 0.40 mg/ml. The total flavonoid content was expressed as mg catechin equivalents per one gram of fresh weight. The radical scavenging activity (RSA) assay was performed after Dobrin et al.[48] The results were expressed in DPPH inhibition percentage. All the solvents used were of analytical grade. The absorbances were measured using the Specord 210 Plus UV/VIS spectro-photometer and all the samples were analysed in triplicates.

RESULTS AND DISCUSSION

The anatomical diversity of wood in the *Moraceae* family is of great systematic significance. The anatomy of *Moraceae* has been studied by many various authors.[49-56] Under different magnifications, slides were studied at the light microscope, and detailed microscopic features of each section of stem, petiole and leaf were noticed.

Stem anatomy

The stem has a circular shape (Figures 1 and 2). A cross-section in a young branch shows an outer epidermis, followed by cortex, which consists of sclerenchyma, collenchyma and parenchyma layers. The pericycle is parenchymatous, being interrupted by small groups of fibres.

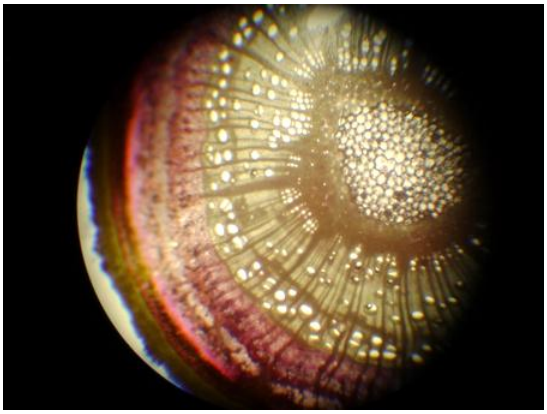

Fig.1. Stem anatomy: cross-section

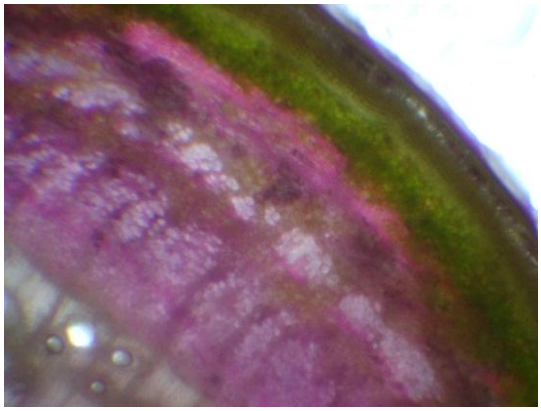

Fig. 2. Details of stem's cross-section

The epidermis of the stem consists of few layers of polygonal cells, covered by a smooth cuticle; the epidermis presents glandular and non - glandular trichomes (Figure 3).

The cortex consists of a continuous layer of 2 - 3 rows of polygonal, isodiametric cells, as well as a collenchyma made up of 5 - 8 cell layers and a paratracheal parenchyma comprising 10 -14 layers of cells. Laticifers are present. Prismatic crystals and druses were observed in the parenchyma (Figure 4). Fibres are thick and elongated (Figure 5). The pericycle is made up of a parenchyma interrupted by groups of lignified fibres. The vascular tissue consists of a continuous ring of outer phloem and inner xylem, showing cambium in between and traversed by medullary rays. *Broussonetia papyrifera* has a porous xylem, ring-shaped, with a distinct ring boundary. The later wood is solitary and contains vessels with helical thickenings. The perforations are simple. The medullary rays are uni or biseriate and they composed of sub rectangular cells with lignified and pitted walls. Rays vary in width and they are 3 to 6 seriate (Figures 6 and 7).

The pith is present in the centre of the stem (Figure 6) and it consists of a somewhat large, rounded, thin-walled parenchyma with narrow intercellular spaces. Inter-vessel pits are non-vestured, alternate, round to polygonal, small. Vessel-ray pits typically have reduced borders to simple, elongate. Prismatic and cluster crystals, laticiferous tubes, as well as tannin cells with brown content are distributed in the phloem and pith tissues.

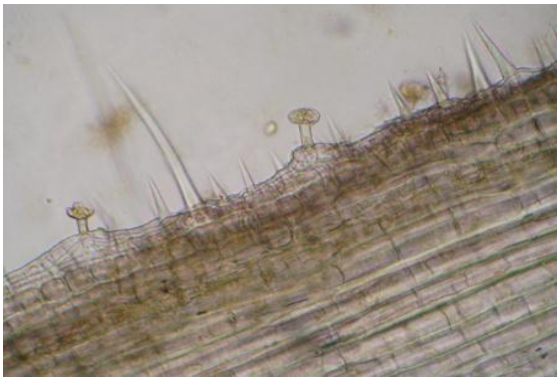

Fig. 3. Longitudinal stem section with glandular and non - glandular trichomes

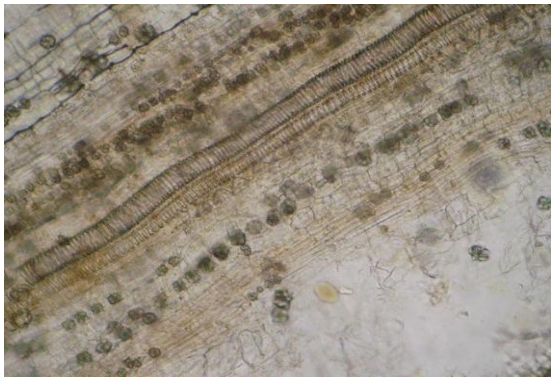

Fig. 4. Longitudinal stem section with vessels and crystals

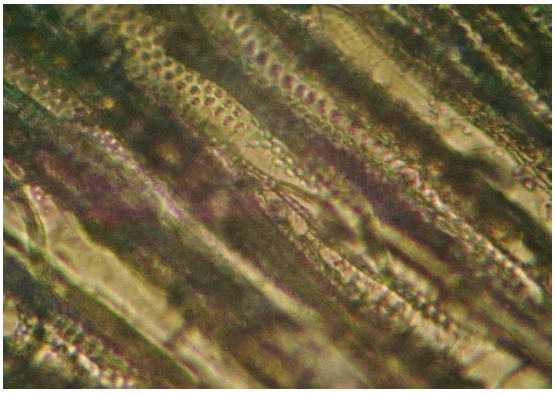

Fig. 5. Longitudinal stem section

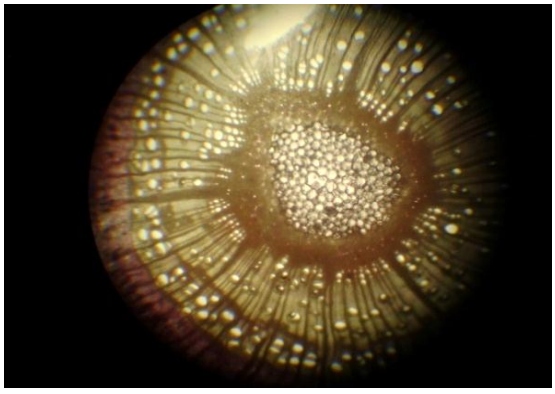

Fig. 6. Cross - section of stem with elongated fibres

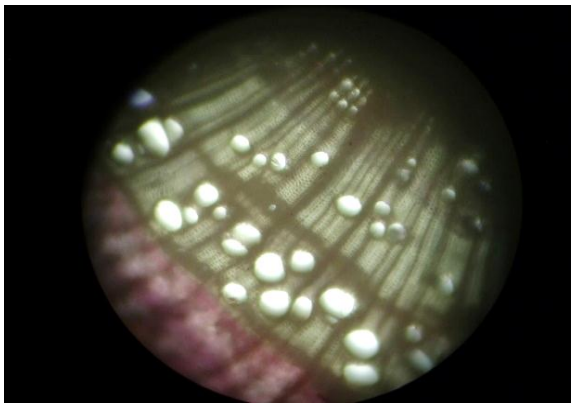

Fig. 7. Ring-shaped xylem with distinct annual ring boundary.

Leaf morphology and macroscopic characteristics

The leaves of *B. papyrifera* are alternate, simple; the petiole up to 2-5 cm long, subtomentose, ovate, puberulous; blade ovate or cordiform or elliptical, 7-12 cm × 5-7.5 cm, entire, rounded or cordate at the base (Figure 8). The lower surface of the young leaves is dense, soft-hairy, pinnately veined, toothed at the margins or crenate - to serrate, dark green on the upper side; female inflorescence is globose, having 1-1.2 cm in diameter; the pedicel is

0.3-1.5 cm long and hairy. Before falling, the leaves roll their halves towards each other on the adaxial surface (Figure 9).

Fig. 8. Leaves of B. papyrifera

Fig. 9. Rolled leaves of B. papyrifera

Petiole anatomy

The cross-section reveals the petiole's epidermis consisting of a single layer of rectangular and oval cells. The epidermis presents glandular and non-glandular trichomes. There is also a cuticle present. Inside there is a sclerenchyma, as well as a parenchyma with 6-13 cell layers. Below the parenchyma there is a cortex whose cells contain crystals and tannins. The vascular bundle has both phloem and xylem (Figures 10 and 11). In the middle of the cross-section there is a ground tissue of the cells of crystals inside.

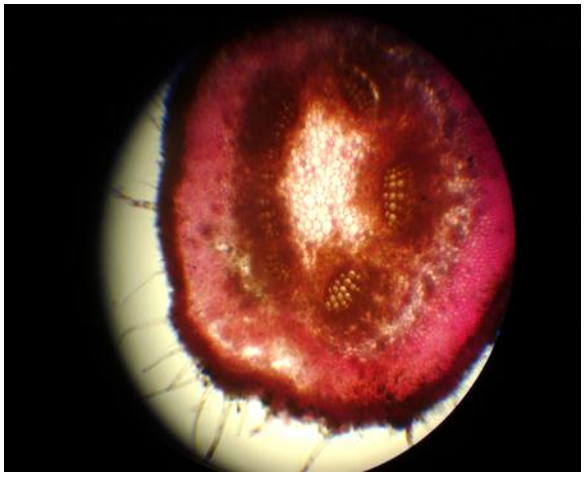

Fig. 10. Petiole's anatomy

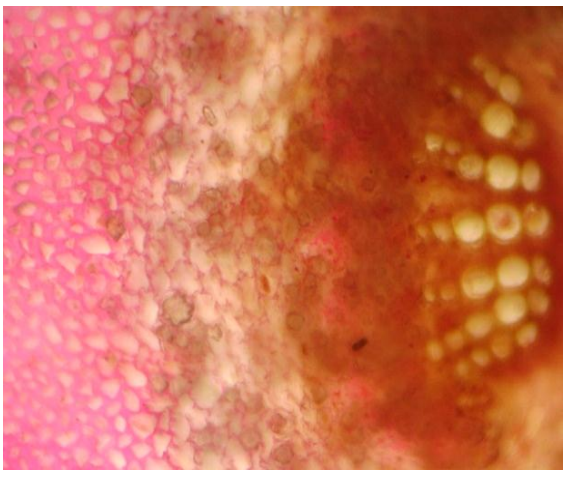

Fig. 11. Crystals and tannins in petiole

Leaf anatomy

The leaves of *B. papyrifera* female plants (Figures 12 and 13) have adaxial and abaxial epidermis, mesophyll and vascular bundle.

Fig. 12. Leaf anatomy - a

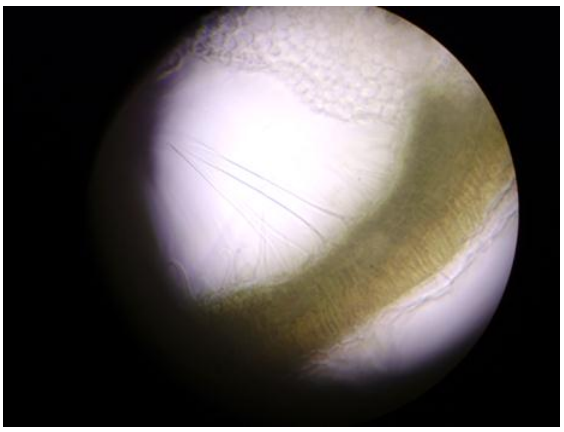

Fig. 13. Leaf anatomy - b

The adaxial (Figures 14 and 15) and abaxial epidermis (Figures 16 and 17) have one layer of cells with thick cuticles and rich in trichomes.

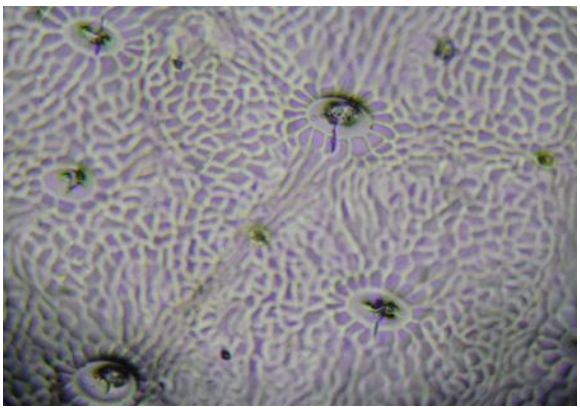

Fig. 14. Adaxial epidermis

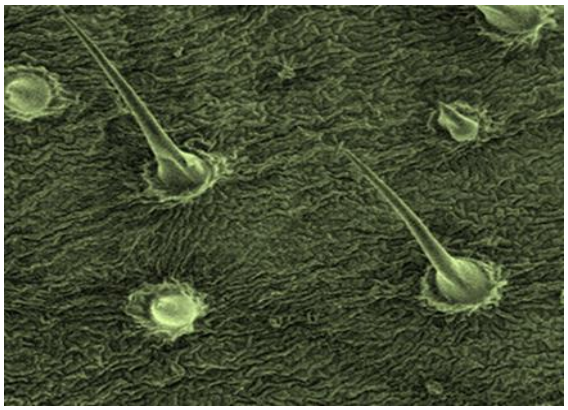

Fig. 15. Adaxial epidermis (SEM)

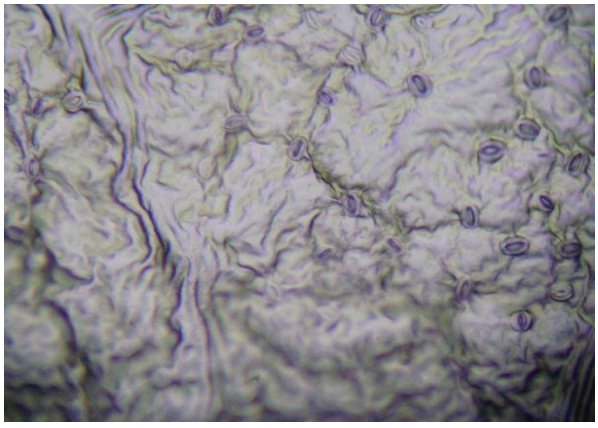

Fig. 16. Adaxial epidermis

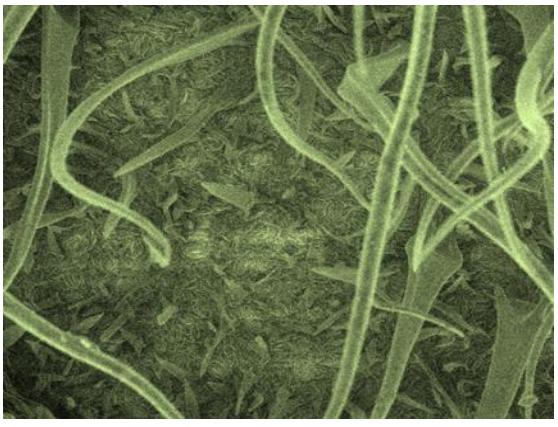

Fig.17. Abaxial epidermis (SEM)

The mesophyll consists of a palisade and a spongy tissue. Sclerenchymatic druses with tannins and crystals are also present in the mesophyll. The laticifers create a network inside the mesophyll, being present on the adaxial side, where the palisade parenchyma is located.

Three types of trichomes are present: glandular, non-glandular and cystolith trichomes.

The glandular trichomes have a short stalk and a spherical head and they are rare on both surfaces. The non-glandular trichomes are unicellular, in various shapes and sizes. They are differentiated into 3 types: large, bristle and bracket. Large trichomes mostly of a conical shape present only on the adaxial surface. Bristle hairs as long clothing trichomes which are characteristic for this species are usually very long and tapering to a narrow point.

Bracket types present simple, ordinary, short with acute or curved tip, densely covered abaxially.

The existence of three types of trichomes has taxonomic value. Trichomes are considered relevant for comparative systematic investigations and for morpho-diagnosis.[57]

Cystolith trichomes are numerous, with large and swollen base and mucronate apex. They are mainly present on the adaxial surface, while stomata appear only on the abaxial epidermis (Figure 17).

Midrib anatomy

The midrib is very prominent on the abaxial surface of the lamina and on the adaxial one.

The midrib is of a fascicular type, consisting of a large arched bundle. Each vascular bundle has a structure similar to that in the petiole. Loosely arranged layers of parenchyma cells without chloroplasts surround the vascular bundle. Fibre cells form adaxial caps only. Laticifers and druses (Figure 19) and trichomes (Figure 20) are also present.

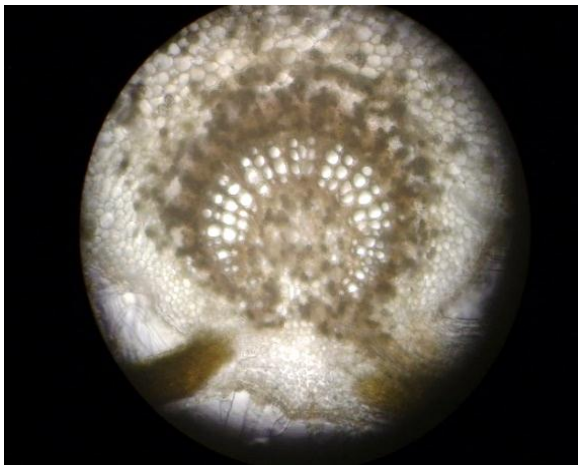

Fig. 19. Midrib

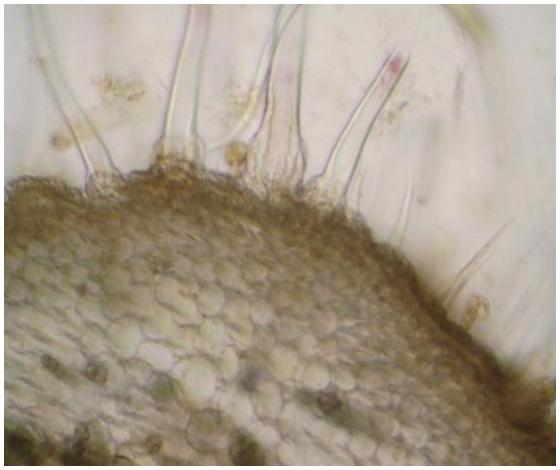

Fig. 20. Trichoms on midrib

Total phenolic analysis (TPA)

The total phenolic assay showed that the *Broussonetia papyrifera* leaves had the highest content (498.13±9.38 mg GAE* / 100 g leaves) than fruits (150.89±1.47 mg GAE / 100 g fruits).

* GAE = gallic acid equivalent

Total flavonoid content (TFC)

Such in case of TPA, the TFC (2.22±0.01 mg of QE/ 100g leaves) was higher than in fruits (0.39 ±0001 mg of QE* / 100g fruits). Among the fresh and fruits ethanol extracts, the leaves extract showed a lower radical scavenging activity (49.90±1.08 %) than fruits: 69.63±1.33 % , Sunt et al. (2012) found an antioxidant activity of 58.11±0.11% in fruits the same researchers found in 2011 antioxidant activity of 62.88% in fruits.

* QE = quercitine equivalent

CONCLUSIONS

The preliminary analysis of EtOH extracts demonstrates that fruits and leaves of *Broussonetia papyrifera* can be sucesssfully used to produce nutritional supplements or as preservative in food products, due to their rich polyphenol content and antioxidant capacity.

The microscopic observations made on leaves, petioles and stems of *Broussonetia papyrifera* showed the presence of many types of trihomes, specific feature of *Moraceae* family.

The morphological and anatomical studies we performed on *Broussonetia papyrifera* stem and leaf cross-sections, as well as on leaf surface sections provide for the first time in our

country valuable information regarding the anatomy of the individuals of *Broussonetia papyrifera* found in Romanian flora.

REFERENCES

1. Clarke, WC, Thaman RR. Agroforestry in the Pacific Islands: Systems and Sustainability. United Nations University Press, Tokyo, Japan, 1993.
2. Wunderlin, RP. Broussonetia l'Héritier ex Ventenat Tabl. Règn. Vég, 1997; 3: 547.
3. Matveeva T, Khafizova G, Sokornova S. In Search of Herbal Anti-SARS-Cov2 Compounds. Front Plant Sci., 2020. doi:10.3389/fpls.2020.589998.
4. Lin LT, Hsu WC, Lin, CC. Antiviral natural products and herbal medicines. Journal of traditional and complementary medicine, 2014; 4(1): 24-35.
5. Lin, CW, Tsai FJ, Tsai CH, Lai CC, Wan L, Ho TY, Chao PDL. Anti-SARS coronavirus 3C-like protease effects of *Isatis indigotica* root and plant-derived phenolic compounds. Antiviral Research, 2005; 68: 36-42.
6. Ghosh R, Chakraborty A, Biswas A, Chowdhuri S. Identification of polyphenols from *Broussonetia papyrifera* as SARS CoV-2 main protease inhibitors using in silico docking and molecular dynamics simulation approaches, J. Biomol. Struct. Dyn., 2020; 1-14. doi: 10.1080/073911 02.2020.1802347.
7. Ryu HW., Lee BW, Curtis-Long MJ., Jung S, Ryu YB., Lee WS., Park KH. Polyphenols from *Broussonetia papyrifera* displaying potent alpha-glucosidase inhibition. Journal of Agricultural and Food Chemistry, 2010; 1: 202-208.
8. Ryu HW., Lee JH., Kang JE, Jin YM, Park KH. Inhibition of xanthine oxidase by phenolic phytochemicals from *Broussonetia papyrifera*. Journal of the Korean Society for Applied Biological Chemistry, 2012; 5: 587-594.
9. Aanouz I, Belhassan A, El-Khatabi K, Lakhlifi T, El-Ldrissi M, Bouachrine M. Moroccan medicinal plants as inhibitors against SARS-CoV-2 main protease: Computational investigations. Journal of Biomolecular Structure and Dynamics, 2020; 1-9.
10. Shree P, Mishra P, Selvaraj C, Singh SK, Chaube R, Garg N, Tripathi YB. Targeting COVID-19 (SARS-CoV-2) main protease through active phytochemicals of ayurvedic medicinal plants - *Withania somnifera* (Ashwagandha), *Tinospora cordifolia* (Giloy) and *Ocimum sanctum* (Tulsi) - a molecular docking study. J Biomol Str. Dyn., 2020; 27: 1-14.
11. Tripathi MK, Singh P, Sharma S, Singh TP, Ethayathulla AS, Kaur P. Identification of bioactive molecule from *Withania somnifera* (Ashwagandha) as SARS-CoV-2 main

protease inhibitor. J. Biomol. Struct. Den., 2020; 1-14. doi: 10.1080/07391102.2020.1790425.

12. Drosten C, Günther S, Preiser W, Van Der Werf S, Brodt HR., Becker S, Berger A. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. N. Engl. J. Med., 2003; 348: 1967-1976.
13. Hoever G, Baltina L, Michaelis M, Kondratenko R, Baltina L, Tolstikov GA, Cinatl J. Antiviral activity of glycyrrhizic acid derivatives against SARS - Coronavirus. J. Med. Chem., 2005; 48: 1256-1259.
14. Gurib-Fakim A. Medicinal plants: traditions of yesterday and drugs of tomorrow. Mol. Asp. Med., 2006; 27: 1-93. doi: 10.1016/j.mam.2005.07.008.
15. Li SY, Chen C, Zhang HQ, Guo HY, Wang H, Wang L, Li RS. Identification of natural compounds with antiviral activities against SARS-associated coronavirus. Antivir. Res., 2005; 67: 18-23.
16. Kim HY, Eo EY, Park H, Kim YC, Park S, Shin HJ, Kim K. Medicinal herbal extracts of *Sophorae radix*, *Acanthopanacis cortex*, *Sanguisorbae radix* and *Torilis fructus* inhibit coronavirus replication in vitro. Antivir. Therap, 2010; 15: 697-709.
17. Hilgenfeld R, Peiris M. From SARS to MERS: 10 years of research on highly pathogenic human coronaviruses. Antivir. Res., 2013; 100, 286-295.
18. Adedeji AO, Sarafianos SG. Antiviral drugs specific for coronaviruses in preclinical development. Current opinion in virology, 2014; 8: 45-53.
19. Park JY, Yuk HJ, Ryu HW, Lim SH, Kim KS, Park KH, Ryu YB, Lee WS. Evaluation of polyphenols from *Broussonetia papyrifera* as Coronavirus protease inhibitors. Journal of enzyme inhibition and medicinal chemistry, 2017; 32(1): 504-515.
20. Dhama K, Khan S, Tiwari R, Sircar S, Bhat S, Malik YS, Singh KP, Chaicumpa W, Bonilla- Aldana DK, Rodrigues - Morales AJ. Coronavirus disease 2019-COVID-19. Clin. Microb. Rev., 2020; 33. doi: 10.1128/CMR.00028-20.
21. Divya M, Vijayakumar S, Chen J, Vaseeharan B, Durán-Lara EF. A review of south Indian medicinal plant has the ability to combat against deadly viruses along with COVID-19 ? Microb. Pathog, 2020. doi: 10.1016/j.micpath.2020.104277.
22. Boukhatem MN, Setzer WN. Aromatic Herbs, Medicinal Plant-Derived Essential Oils and Phytochemical Extracts as Potential Therapies for Coronaviruses: Future Perspectives, Plants, 2020; 9(6): 800.

23. Boukhatem MN, Setzer WN. Covid-19 outbreak: is there a place for natural remedies and herbal medicines? Pharmacopée traditionnelle et Covid-19 : faut-il compter sur les herbes aromatiques et les plantes médicinales ? Revue Agrobiologia, 2020; 10(1): 1731-1738.
24. Wu WT. Evaluation of anti-inflammatory effects of *Broussonetia papyrifera* stem bark, Indian J. Of Pharmac, 2012; 44(1): 26-30.
25. Lee D, Bhat KP, Fong HH, Farnsworth NR, Pezzuto JM, Kinghorn AD. Aromatase inhibitors from *Broussonetia papyrifera*. Journal of Natural Products, 2001; 64: 1286-1293.
26. Lee JM, Choi SS, Park MH, Jang H, Lee YH, Khim KW, Oh SR, Park J, Ryu HW, Choi JH. *Broussonetia papyrifera* root bark extract exhibits anti-inflammatory effects on adipose tissue and improves insulin sensitivity potentially via AMPK activation. Nutrients, 2020; 14(12(3)): 773.
27. Narkhede RR, Pise AV, Cheke RS, Shinde SD. Recognition of natural products as potential inhibitors of COVID-19 main protease (Mpro): In-Silico Evidences. Nat Prod Bioprospect, 2020; 10(5): 297-306.
28. Calixto J.B. "Twenty-five years of research on medicinal plants in Latin America: a personal view," Journal of Ethnopharmacology, 2005; 100(1-2): 131-134.
29. Duke JA, Ayensu ES. Medicinal Plants of China. 2 Vols. 705 S., 1300 Strichzeichnungen. Reference Publ., Inc. Algonac. Michigan Press: Geb. M., 1985. ISBN 0-917266-20-4.
30. Sun J, Liu SF, Zhang CS, Yu LN, Bi J, Zhu F, Yang QL. Chemical composition and antioxidant activities of *Broussonetia papyrifera* Fruits. Plus One, 2012; 7(2). https://doi.org/ 10.1371/journal.pone.0032021.
31. Sun J, Zhang CS, Yu LN, Bi J, Liu SF, Zhu F, Yang Q.L. Antioxidant activity and total phenolics of *Broussonetia papyrifera* flower extracts. Applied Mechanics & Materials, 2011; 140: 263-267.
32. Fang SC, Shieh BJ, Wu RR, Lin CN. Isoprenylated flavonols of formosan *Broussonetia papyrifera*. Phytochemistry, 1995; 38(2): 535-537.
33. Lin CN, Lu CM, Lin HC, Fang SC, Shieh BJ, Hsu MF, Wang JP, Ko FN, Teng CM. Novel antiplatelet constituents from formosan moraceous plants. J. of Nat. Products, 1996; 59(9): 834-838.
34. Ko HH, Yu SM, Ko FN, Teng CM, Lin CN. Bioactive constituents of *Morus australis* and *Broussonetia papyrifera*. Journal of Natural Products, 1997; 60: 1008-1011.

35. Son KH, Kwon SJ, Chang HW, Kim HP, Kang SS. Papyriflavonol A, a new prenylated flavanol from *Broussonetia papyrifera*. Fitoterapia, 2001; 72(4): 456-458.
36. Chen RM, Hu LH, Ann TY, Li J, Shen Q. Natural PTP1B inhibitors from *Broussonetia papyrifera*. Bioorganic & Medicinal Chemistry Letters, Dec., 2002; 12(23): 3387-3390. DOI: 10.1016/s0960-894 x (02)00757-6.
37. Vasanth N, Melchias G, Kumaravel P. Biogenic silver nanoparticles mediated by *Broussonetia papyrifera*: Anticancer and antimicrobial activity against pathogenic organisms, Asian Journal of Pharmaceutical and Clinical Research, 2017; 10(5): 93.
38. Si B, Tao H, Zhang X, Guo J, Cui K, Tu Y, Diao Q. Effect of *Broussonetia papyrifera L*. (paper mulberry) silage on dry matter intake, milk composition, antioxidant capacity and milk fatty acid profile in dairy cows. Asian-Australas J. Anim. Sci., Aug, 2018; 31(8): 1259-1266.
39. Jeong JH, Ryu JH. Broussoflavonol B from *Broussonetia kazinoki Siebold* exerts anti-pancreatic cancer activity through downregulating FoxM1. Molecules, 2020; 16; 25(10): 2328.
40. Anwar T, Jabbar A, Khalique F, Tahir S, Shakeel MA. Plants with insecticidal activities against four major insect pests in Pakistan. Tropical Pest Management, 1992; 38(4): 431-437.
41. Shirata A, Takahasi K. Production and accumulation of antifungal substances in xylem tissue of shoots of plants belonging to *Moraceae*. Annals of Phytopath. Soc. of Japan, 1979; 452: 156-161.
42. Bhardwaj VK, Singh R, Sharma J, Rajendran V, Purohit R, Kumar S. Identification of bioactive molecules from tea plant as SARS-CoV-2 main protease inhibitors. Journal of Biomolecular Structure and Dynamics, 2020; 1-10.
43. Ghosh R, Chakraborty A, Biswas A, Chowdhuri S. Evaluation of green tea polyphenols as novel coronavirus (SARS CoV-2) main protease (Mpro) inhibitors - an in silico docking and molecular dynamics simulation study. J Biomol Struct Dyn, 2020; 1-13. doi: 10.1074/jbc.M310875200.
44. Luo H, Tang QL, Shang YX, Liang SB, Yang M, Robinson N, Liu JP. Can Chinese medicine be used for prevention of coronavirus disease 2019 (COVID-19)? A review of historical classics, research evidence and current prevention programs. Chinese. J. Int. Med., 2020; 26: 1-8.
45. Danaatmadja O. Saeh (*Broussonetia papyrifera Vent*.) as raw material for luxurious hand-made paper. Duta Rimba, 1992; 18(141-142): 14-17.

46. Huang H, Zhao Y, Xu Z, Zhang W, Jiang K. Physiological responses of *Broussonetia papyrifera* to manganese stress, a candidate plant for phytoremediation. Ecotoxic. Envir. Saf., 2019; 181: 18-25.
47. Luchian V, Georgescu MI, Savulescu E, Popa V. Some aspects of morpho-anatomical features of the invasive species *Eleusine indica (L.) Gaertn*. Scientific Papers. Series A. Agronomy, 2019; LXII: 1. ISSN CD-ROM 2285-5793; ISSN Online 2285-5807; ISSN-L 2285-5785.
48. Dobrin A, Popa VI, Potor CD, Georgescu MI. Phytochemical research on aerial parts of *Raphanus raphanistrum subsp. landra* (Moretti ex D.C.) Bonnier & Layens Publishing House. Scientific Papers-series A-Agronomy, Jan 1, 2018; 61: 458-63.
49. Azizian D, Sonboli A. Leaf anatomy and micro-morphology of the genus *Ficus* Iran. Journal of Botany 9 (2), 2002 L. (Moraceae). Iran. Jour. Biology, 1999; 8-4: 14-93.
50. Azizian D. Morphology and distribution of trichomes in some genera (*Morus, Ficus, Broussonetia* and *Maclura*) of *Moraceae* in Iran. Iran. Journal of Botany, 2002; 9(2): 195-202.
51. Gangadhara M, Inamdar IA. Trichomes and stomata and their taxonomic significance in the *Urticales* - Plant. Syst. Evol., 1977; 127: 21-137.
52. Metcalfe CR, Chalk L. Anatomy of Dicotyledons vol. II. *Moraceae.* Clarendon Press, Oxford, 1950; 1259-1271.
53. Metcalfe CR, Chalk L. Anatomy of the Dicotyledons, Vol. 1, 2nd edition, Clarendon Press, Oxford, 1988; 100-106.
54. Shah AM, Kachroo P. Comparative anatomy in Urticales. The trichomes in *Moraceae.* Jour. Ind. Bot. Soc., 1975; 54: 138-153.
55. Hardin J. Atlas of foliar surface features in woody plants, II. *Broussonetia*, *Morus*, and *Maclura* of North America. Bulletin of the Torrey Botanical Club, 1981; 108(3): 338-346. doi:10.2307/2484713.
56. Wu CC, Kuo-Huang, LL. Calcium crystals in the leaves of some species of *Moraceae*, 1Bot. Bull. Acad. Sin., 1997; 38: 97-104 97.
57. Bercu R, Bavaru E. Morphological and morphometrical characterisation of some *Ficus L.* species leaf, Analele Universităţii „Ovidius", Seria: Biologie-Ecologie, 2003; 7: 9-16.
58. Berg CC, Corner EJH, Jarrett FM. Flora Malesiana - *Moraceae* genera other than *Ficus.*, Series I, 2006; 17/Part 1: 1-152.
59. Shakir H, Baji SH. Anatomical study of some characters in certain species of genus *Ficus L.* growing in Iraq. Journal of Biology, Agriculture and Healthcare, 2016; 6: 98-105.

60. Schnetzler BN, Teixeira SP, Marinho CR. Trichomes that secrete substances of a mixed nature in the vegetative and reproductive organs of some species of *Moraceae*, Acta Botanica Brasilica, 2017; 31(3): 392-402.