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Bekul Fruit, Potential Pharma food from Northern Region of Bali Island, Indonesia: Selected Phytochemical Analyses and Antioxidant Activity of Its Ethanol Extract

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Bekulfruit from Northern region (Buleleng regency), Bali, Indonesia, is commonly consumed fresh in the island of Bali or processed as local delicacy and used as part of religious offerings. Up to date, there is no data regarding the taxonomy, phytochemical composition, and antioxidant properties of this Balinese fruit. This study was aimed to investigate total phenolic content, tannin content and antioxidant activity of the ethanol extract of bekul fruit obtained from Banjar district, Buleleng regency, Bali. Total phenolic compound was quantified in terms of gallic acid equivalent (GAE) by using Folin-Ciocalteu method, meanwhile tannin content was determined in terms of tannic acid equivalent (TAE). IC_{50} of the extract was determined using DPPH assay, and subsequently used in the calculation of antioxidant activity index (AAI) using the formula of Scherer and Godoy (2009). Bekul plant was revealed as *Ziziphusjujuba* Mill. Total phenolic and tannin content of the extract was 29.48 mg/100 g GAE and 91.06 mg/100 g TAE, respectively. Thevalue of IC50was 77.40 mg/ml, with antioxidant activity index (AAI) of 50.94. Ethanol extract of bekul(*Ziziphusjujuba* Mill.) fruit contains phenolic and tannin compounds. This extract is found to scavenge free radicals and possess very strong antioxidant activity*in vitro*. Taken together, these findings lead to the notion that bekul fruit from Northern region of Bali, Indonesia, is a promising pharma food.

Keywords: *Ziziphusjujuba* Mill.fruit, Ethanol extract, Total phenolics, Tannins, Antioxidant activity.

Endogenous antioxidant system is deployed by human body to mitigate the adverse effects of oxidative stress, thus maintaining the homeostasis. Unfortunately, in many pathological conditions, this system of mitigation is frequently overwhelmed and subsequently contribute to the genesis and progressivity of many diseases. Supplementation of exogenous antioxidants in these situations will enhance the capacity of human body to attenuate oxidative stress and restore the homeostasis, as reviewed elsewhere.[1] Natural products such as fresh fruits have long been known as good sources of exogenous antioxidants.[2]

A local fruit known in Bali as bekul fruit has not been investigated for its biomedical potentials, especially as a source of antioxidants. North Balinese *bekul* fruit, cultivated in Banjar District, Buleleng Regency, Bali, Indonesia is

variable in size and tastes sweet with a hint of sourness. The skin is green and glossy, similar to that of Malang apple from East Java region, Java, Indonesia. The fruit is usually eaten immediately after harvest under fresh condition, or mixed with a special sauce (shrimp paste-based sauce) and made into local delicacy known as *rujakbekul*(a kind of Indonesian traditional spicy salad with bekul fruit as its main ingredient). The fruit is also used as part of offerings in Balinese Hindu (Sanatana Dharma) religious ceremonies. Thus, bekul fruit is mainly used for local consumption and for religious purpose.

To the best of our knowledge, there is lack of information regarding the taxonomy, phytochemical composition, and antioxidant activity of North Balinese bekul fruit. Therefore, it is important to determine the species and investigate selected phytochemical properties of bekul fruit cultivated in North Bali. Specifically, a study on taxonomy, selected phytochemical constituents and antioxidant activity of North Balinese bekulfruit ethanol extract was conducted as an initial effort to explore its potential biomedical benefits.

MATERIALS AND METHODS

Species Determination

The whole live plant was obtained from a local bekul plantation in Banjar, Buleleng regency (North Bali region) and submitted to the office of *Lembaga Ilmu Pengetahuan Indonesia*/LIPI (Indonesian Institute of Sciences) at EkaKarya Bali Botanical Garden, Bedugul, Tabanan regency, Bali, for taxonomical analysis. The process of identification was done by three official botanists/ taxonomists of LIPI. The plant was then kept in the botanical garden as trophy or voucher specimen.

Extraction of Bekul Fruit

Bekul fruits were air-dried and macerated in 80% ethyl alcohol for 48 hours. The macerate was then subjected to evaporation for removing water content, using a rotary vacuum evaporator. All procedures were done in Laboratory of Pharmacology and Therapy/Division of Drug Development and Laboratory Animal, Integrated Biomedical Laboratory Unit, Faculty of Medicine, Udayana University, Denpasar, Bali.

Total Phenolic and Tannin Content Analyses

Folin-Ciocalteu method was used in quantifying total phenolic content of bekul fruit ethanolic extract, as described in our previous study. A part (100 mg) of the extract was dissolved in 85% methyl alcohol, and then subjected to vortex and filtration. The resulting filtrate and standard solution were mixed respectively with Folin-Ciocalteureagent and vortexed. The solutions were rested for 6 minutes and then mixed with 0.8 mL of 5% Na_2CO_3, vortexed and allowed to rest again for 30 minutes. These steps produced blue colour. The absorbances were measured at 760 nm. Linear regression curves were made to determine the formula y = ax + b, based on the absorbances and concentrations. The phenolic content of the sample was expressed as gallic acid equivalent (GAE) per gram of dry weight of the sample. UV-Vis spectrophotometry was used in the quantification of phenolics and tannins of bekul fruit ethanolic extract. Tannin content was expressed as tannic acid equivalent (TAE). Quantitative phytochemical analyses were done in Laboratory of Food Analysis, Universitas Udayana, Denpasar, Bali.

Determination of Antioxidant Activity

The assay we used in determining antioxidant activity of the extract is a slightly-modified version of the assay done by Aldarraji *et al*.,[3] as described previously in Dewi *et al*.[4]Five concentrations of the sample were made using methyl alcohol as solvent. Each 100 mL of sample was mixed with 700 mL DPPH solution (0.1 mM), shaken well, and then incubated for 30 minutes in dark room (RT).Gallic acid was used as positive control. The absorbance values were read at wavelength of 517 nm. Percentage of DPPH free radical inhibition by the extract was calculated using the formula:

$$\text{Inhibition (\%)} = \frac{A_{control} - A_{sample}}{A_{control}} \times 100 \quad ...(1)$$

The results were made into a graph to obtain the linear regression equation and IC_{50} value. The antioxidant activity of the extract is expressed as antioxidant activity index (AAI), calculated using formula proposed by Scherer and Godoy[5]:

$$AAI = \frac{\text{Final concentration of DPPH } (\mu g/ml)}{IC_{50}\ (\mu g/ml)} \quad ...(2)$$

Interpretation of AAI value was done based on the category proposed by Scherer and Godoy.[5]A test substance was considered to have poor antioxidant activity if AAI < 0.5, moderate antioxidant activity if between AAI is 0.5-1.0, strong antioxidant activity if AAI 1.0-2.0, and very strong when AAI > 2.0.

RESULTS

Plant Identification

The result of species identification is presented in Table 1. The certificate of the determination/identification was issued by Head of Exploration and Collection of Plants, EkaKarya Bali Botanical Garden – LIPI (certificate number: B-37/IPH.7/AP/I/2018).

Table 1. The Taxonomy of *Bekul*

Kingdom	*Plantae*
Division	*Spermatophyte*
Subdivision	*Angiospermae*
Class	*Dicotyledonae*
Order	*Rosales*
Family	*Rhamnaceae*
Genus	*Ziziphus*
Species	*Ziziphusjujuba* Mill.

Total Phenolic Content

The result of absorbance measurement for different concentrations of the sample is presented in Figure 1.

Total Tannin Content

The measurement of total tannin content was based on the reagent manufacturer's standard (Sigma Aldrich). The procedure was initiated by making extract preparations having different concentrations. The result of tannin analysis is shown in Figure 2. The regression (r) value was found to be 0.9742 (with y = 0.114x + 0.0957).

Free Radical Scavenging Activity and Antioxidant Activity Index

Free radical scavenging capacity of bekulethanolic extract had been measured using 2,2 diphenyl-1-pycrilhidrazyl(DPPH) assay, and calculated using Formula 1. The IC_{50}values were obtained from linear regression analysis of inhibition DPPH 0.1 mM. In this study, we obtained regression % inhibition y=0.6934x – 0.5106 with correlation coefficient value of 0.9485. The results of DPPH free radical scavenging activity and AAI

Table 2. IC_{50} and AAI of *Bekul* (*Ziziphusjujuba* Mill.) Fruit Ethanol Extract

Parameters of Antioxidant Properties	
IC_{50}	AAI
77.40 µg/ml	50,94

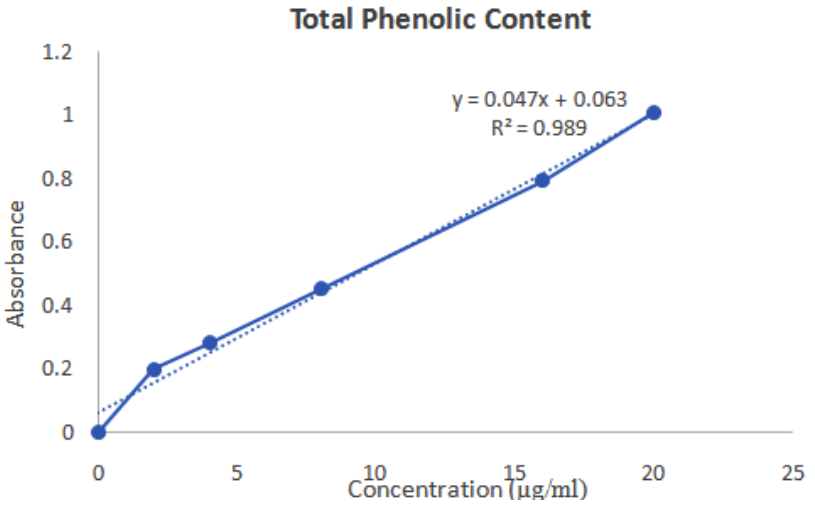

Fig. 1. Concentration versus absorbance at 760 nm wavelength

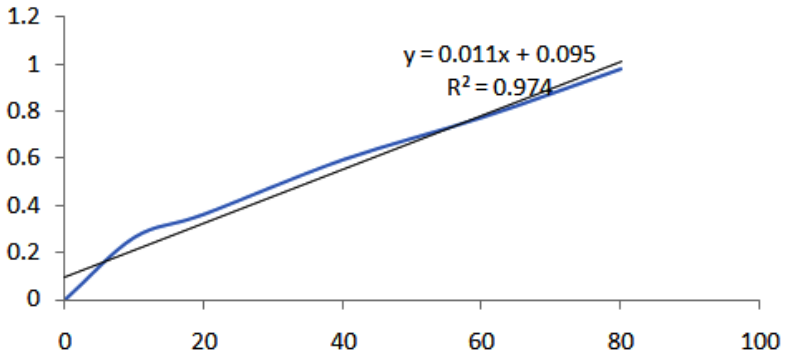

Fig. 2. Calibration curve of Total Tannins of Bekul Ethanol Extract

quantification (based on calculation using formula 2) are shown in Table 2.

DISCUSSION

In current study, we aimed to reveal the taxonomy of North Balinese bekul, and to investigate total phenolics, tannin content and assessing *in vitro*antioxidant activity of bekul fruit ethanol extract. Taxonomically, *Ziziphus jujube* Mill. was revealed as the scientific name of bekul. This species is known as Asian native plant.[6]Several relatives of bekul(*Z. jujube* Mill.) have been studied phytochemically, namely, *Z. lotus*, *Z. mauritiana*, *Z. mucronata*, *Z. spina-christi* and *Z. xylopylorus*. Bioactive phyto components and biomedicinal potentials of *Z. jujube* Mill. fruit had been discussed elsewhere.[7]In a recent review, *Z. jujube* Mill. fruit is known to be ethnopharmaceutically used in China to treat blood deficiency (as "Qi" tonifier), and had been discussed both as a prophylactic and therapeutic natural product to combat anemia.[8]

Quantitative phytochemical analysis revealed that bekul ethanol extract contained phenolicsas much as29.48 mg/100 g gallic acid equivalent (GAE). Total phenols content in our study was much lower than that of 7 cultivars of Chinese *Z. jujube* fruit ethanol extract.[9] This difference may be caused partly by the concentration of the ethanol used during the extraction. The ethanol concentration in our study was lower that of Zhao *et al*., i.e., 80% versus 95%, respectively.[9]The ethanol extract of *Z. spina-christi* fruit from Oman was also shown to contain phenolic compounds and exhibit sound *in vitro* anti-inflammatory activity, compared to diclofenac sodium.[10]Fruit from other species, i.e., *Z.mauritiana* obtained from Nigeria had been also shown to contain phenolic content, with higher amount than the specimen in our study. Total phenolic compounds from *Z. mauritiana* fruit aqueous extract was found to be 402.31±53.6mg GAE/100g.[11]Methanol extract of *Z. xylopylorus* fruit from Karnataka, India, was observed to contain 6262 mg GAE/100g.[12]The findings confirm that species and biogeographical factors are important determinants of secondary metabolite content, especially total phenolic compounds found in plants. The use of different solvents is also an important factor in determining the amount of extracted bioactive substances.

Tannin content in bekul fruit ethanol extract was revealed to be 91.06 mg/100 g TAE. Tannins in fruits of many plant species are a group protective compounds that act to protect plants against wide array of phytopathogens.[13]Condensed tannins (and flavanols) are assumed to take predominant role in determining the antioxidant activity of ripe *Z. mauritiana* Lamk fruit.[14]Since ripe bekul(*Ziziphus jujube* Mill.) fruits were used in current study, tannins may be assumed to contribute significantly to the antioxidant activity of its ethanol extract. There is currently lack of data regarding tannins content of *Z. jujube* Mill. fruit ethanol extract, using tannic acid as standard in the determination of tannin content. To tackle this issue we compare our result of tannin content determination to the findings of phytochemical (tannins) study on the relative of *Z. jujube* Mill., such as *Z. mauritiana* Lam. Similar to our finding, tannins is also present in ripe *Z. mauritiana* Lam. fruit obtained from Madya Pradesh, India. The ethanol extract of this Indian fruit was known

to present in high amount (4+), but the exact amount awaits further investigation.[15]Fruit juice of *Z. lotus* was also revealed to contain both condensed and hydrolysable tannins.[16] Moreover, proanthocyanidins (condensed tannins) is present in the ethanol extract of another part of genus *Ziziphus*, such as shown in of *Z. mucronata* Willd. subsp. *mucronata* Willd bark.[17]

Bekul fruitethanol extract was showed to exhibitIC50 value of 77.40 µg/ml and very strong antioxidant activity (AAI > 2.0). Our specimen exhibited lower DPPH free radical scavenging activity than methanol extract of *Z. xylopylorus*(Retz.) Willd. from Karnataka, India showed IC50 value 36.79µg/ml,[12]but higher activity than the extract of Nigerian *Ziziphusmauritiana* fruit (IC50 value = 338.45ìg/ml).[11]Bekul fruit ethanol extract was revealed to possess very strong antioxidant activity, based on the AAI value. Phenolics and tannins are secondary metabolites that ubiquitously exist in plants and their fruits.[18,19]In current study, phenolic compounds and tanninsmay contribute synergistically to the significant *in vitro*antioxidant activity of *bekul* (*Ziziphus jujube* Mill.) ethanol extract.

It is possible that other parts of bekul plant may also contain significant amount of phenolic compounds and other bioactive substances. Choi *et al*. found that South Korean *Z. jujube* seeds fractionated using different solvents exhibited substantial amount of total phenolics (ranging from 7,90 $\pm$ 0,47 mg GAE/g to 102,05 $\pm$ 2,42 mg GAE/g fraction).[20]Both of our findings and that of Choi *et al*.[20]promote the importance of conducting comparative phytochemical studies on various parts of North Balinese bekul plant, applying various solvents in the extraction process. Other factor that can be attributed to the variation of phytochemical composition, is the ripening stage of fruit. A study revealed that phenolic and tannin profiles of *Z. mauritiana* Lamk fruits can be influenced by ripening or maturation stage.[14] Therefore, it is also essential to consider this factor in studying the phytochemical composition of various parts of North Balinesebekul plant.

In order to be incorporated safely in clinical practice, a natural product mustnot be proved as genotoxic agent. Genotoxicity is a disruptive feature of an agent that may cause damage to DNA and/or cytocomponents that regulate the behaviour and functions of chromosomes.[21]Recently, Indian *Z. jujuba* fruit ethanol extract had been known to exhibit non-genotoxicity, both *in vitro* and *in vivo*. Moreover, the extract had been also revealed to attenuate DNA alkylation *in vivo*,[22] thus can be viewed as a phyto-antigenotoxin. The findings can be considered as preliminary signs of promising application in clinical settings, especially in the context of therapeutic safety. It is mandatory to extend this type of study in clinical settings to elucidate the safety profile of *Z. jujube*Mill. fruit extract before assessing its health-promoting efficacy in humans.

Attenuated amount of endogenous antioxidants may predisposehuman body to oxidative stress and its associated damages. Oxidative stressis known to play significant roles inpathological entities such as cardiovascular disease (CVD), acute and chronic kidney disease (CKD), neurogenerative diseases (NDs), diabetes and cancer.[23]Oxidative stress is also known tobe associated with inflammaging ina diverse array of pathological states, as reviewed elsewhere.[24]Since oxidative stress is linked to many crippling health problems, it is important to adhere to healthy life style to promote health and halt the progression of diseases. One of the most convenient health-promoting ways is to consume natural products, such as fruits rich in antioxidants or high in antioxidant activity. Bekul (*Z. jujube* Mill.) fruit from northern region of Bali, Indonesia,is a promising example of such natural products.

CONCLUSION

North Balinese bekul was found to be *Ziziphus jujube* Mill. The ethanol extract of its fruit had been revealed to possess phenolic compounds and tannins. The extract also exhibited free radical scavenging activity and very strong antioxidant property, based on DPPH assay and AAI value, respectively. Taken together, these findings indicate that bekulfruit from Northernregion of Bali, Indonesia, is a pharma food with promising antioxidant activity.

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Conflict of interest

The authors declare that they do not have any conflict of interest.

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REFERENCES

1. Kurutas EB. The importance of antioxidants which play the role in cellular response against oxidative/nitrosative stress: Current state. *Nutrition Journal*. (2016). https://doi.org/10.1186/s12937-016-0186-5
2. Xu DP, Li Y, Meng X, Zhou T, Zhou Y, Zheng J, *et al*. Natural antioxidants in foods and medicinal plants: Extraction, assessment and resources. *International Journal of Molecular Sciences*. (2017). https://doi.org/10.3390/ijms18010096
3. Aldarraji Q, Halimoon N, Majid N. Antioxidant activity and total phenolic content of earthworm paste of Lumbricus rubellus (red worm) and Eudrilus eugenia (African night crawler). J Entomol Nematol [Internet]. **5**(3):33–7 (2013). Available from: https://www.researchgate.net/publication/264159663_Antioxidant_activity_and_total_phenolic_content_of_earthworm_paste_of_Lumbricus_rubellus_red_worm_and_Eudrilus_eugenia_African_night_crawler doi: 10.5897/JEN2013.0075
4. Dewi NWS, Mahendra AN, Putra GWK, Jawi IM, Sukrama DM, Kartini NL. Ethanolic extract of the powder of red earthworm (Lumbricus rubellus) obtained from several organic farmlands in Bali, Indonesia: Analysis of total phenolic content and antioxidant capacity. *Bali Med J*. (2017) https://doi.org/10.15562/bmj.v6i3.730
5. Scherer R, Godoy HT. Antioxidant activity index (AAI) by the 2,2-diphenyl-1-picrylhydrazyl method. Food Chem [Internet]. **112**(3):654–658 (2009). Available from: https://www.sciencedirect.com/science/article/abs/pii/S0308814608007218 doi: https://doi.org/10.1016/j.foodchem.2008.06.026
6. Jin X. Jujuba— Ziziphus jujuba. In: *Exotic Fruits* (2018). https://doi.org/10.1016/b978-0-12-803138-4.00034-4
7. Gao Q-H, Wu C-S, Wang M. The Jujube (Ziziphus Jujuba Mill.) Fruit: A Review of Current Knowledge of Fruit Composition and Health Benefits. *J Agric Food Chem* [Internet]. **61**(14):3351"3363 (2013). Available from: https://pubmed.ncbi.nlm.nih.gov/23480594/ doi: 10.1021/jf4007032
8. Chen J, Tsim KWK. A Review of Edible Jujube, the Ziziphus jujuba Fruit: A Heath Food Supplement for Anemia Prevalence. *Front Pharmacol* [Internet].; **11**:1–12 (2020). Available from: https://pubmed.ncbi.nlm.nih.gov/33324222/ doi: 10.3389/fphar.2020.593655
9. Zhao H, Zhang H, Yang S. Phenolic compounds and its antioxidant activities in ethanolicextracts from seven cultivars of Chinese jujube. *Food Sci Hum Wellness* [Internet]; **3**(3–4):183–90 (2014). Available from: https://www.sciencedirect.com/science/article/pii/S2213453015000038 doi: https://doi.org/10.1016/j.fshw.2014.12.005
10. Alhakmani F, Khan SA, Ahmad A. Determination of total phenol, in-vitro antioxidant and anti-inflammatory activity of seeds and fruits of Zizyphus spina-christi grown in Oman. *Asian Pac J Trop Biomed* [Internet]; **4**(Suppl 2):S656–60 (2014). Available from: https://www.sciencedirect.com/science/article/pii/S2221169115300666 doi: 10.12980/APJTB.4.2014APJTB-2014-0273
11. Okala A, Ladan M, Wasagu R, Shehu K. Phytochemical Studies and In Vitro Antioxidant Properties of Ziziphus mauritiana Fruit Extract. *Int J Pharmacogn Phytochem Res.*; **6**(4):885–8 (2014).
12. Raghavendra H, Prashith K, Akarsh S, Ashwini H. Phytochemical Analysis, Antifungal and Antioxidant Activity of Leaf and Fruit of Zizyphus xylopyrus (Retz.) Willd. (Rhamnaceae). *Sci Technol Arts Res J* [Internet]; **4**(4):83–8 (2015). Available from: https://www.ajol.info/index.php/star/article/view/145824 doi: http://dx.doi.org/10.4314/star.v4i4.12
13. Yahia Y, Benabderrahim, Mohamed Ali Tlili N, Bagues M, Nagaz K. Bioactive compounds, antioxidant and antimicrobial activities of extracts from different plant parts of two Ziziphus Mill. species. *PLoS One* [Internet]; **15**(5):1–16 (2020). Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0232599 doi: 10.1371/journal.pone.0232599
14. Suzie Z, Adrien S, Guillaume C, Didier

M-A-M, Sylvie R, Dominique P, *et al*. Changes in antioxidant activity during the ripening of Jujube (Ziziphus mauritiana Lamk). *Food Chem* [Internet]. **150**:448–56 (2013). Available from: https://pubmed.ncbi.nlm.nih.gov/24360474/ doi: : 10.1016/j.foodchem.2013.11.022

15. Rathore SK, Bhatt S, Dhyani DS, Jain A. Preliminary Phytochemical Screening of Medicinal Plant Ziziphus mauritiana Lam. Fruits. *Int J Curr Pharm Res* [Internet]; **4**(3):160–2 (2012). Available from: https://www.researchgate.net/publication/281377329_Preliminary_phytochemical_screening_of_medicinal_plant_Ziziphus_mauritiana_Lam_fruits
16. Benidir M, El Massoudi S, El Ghadraoui L, Lazraq A, Benjelloun M, Errachidi F. Study of Nutritional and Organoleptic Quality of Formulated Juices from Jujube (Ziziphus lotus L.) and Dates (Phoenix dactylifera L.) Fruits. *Sci World J* [Internet]. 2020; 2020:1–9. Available from: https://pubmed.ncbi.nlm.nih.gov/32292296/ doi: 10.1155/2020/9872185
17. Olajuyigbe OO, Afolayan AJ. Phenolic content and antioxidant property of the bark extracts of Ziziphus mucronata Willd. subsp. mucronata Willd. *BMC Complement Altern Med* [Internet]; **11**(130):1–8 (2011). Available from: https://pubmed.ncbi.nlm.nih.gov/22176659/ doi: 10.1186/1472-6882-11-130
18. Brglez Mojzer E, Knez Hrnèiè M, Škerget M, Knez Ž, Bren U. Polyphenols: Extraction Methods, Antioxidative Action, Bioavailability and Anticarcinogenic Effects. Molecules (Basel, Switzerland). 2016. https://doi.org/10.3390/molecules21070901
19. Montes-Ávila J, López-Angulo G, Delgado-Vargas F. Tannins in fruits and vegetables: Chemistry and biological functions. In: Fruit and Vegetable Phytochemicals: Chemistry and Human Health: Second Edition. 2017. https://doi.org/10.1002/9781119158042.ch13
20. Choi J, An X, Lee BH, Lee JS, Heo HJ, Kim T, *et al*. Protective Effects of Bioactive Phenolics from Jujube (Ziziphus jujuba) Seeds against H2O2–induced Oxidative Stress in Neuronal PC-12 Cells. *Food Sci Biotechnol* [Internet]; **24**(6):2219–27 (2015). Available from: https://link.springer.com/article/10.1007/s10068-015-0296-4 doi: https://doi.org/10.1007/s10068-015-0296-4
21. López-Romero D, Izquierdo-Vega JA, Morales-González JA, Madrigal-Bujaidar E, Chamorro-Cevallos G, Sánchez-Gutiérrez M, *et al*. Evidence of Some Natural Products with Antigenotoxic Effects. Part 2: Plants, Vegetables, and Natural Resin. *Nutrients* [Internet]. **10**(12):1–46 (2018). Available from: https://pubmed.ncbi.nlm.nih.gov/30544726/ doi: 10.3390/nu10121954
22. Goswami P, Banerjee R, Mukherjee A. Potential antigenotoxicity assessment of Ziziphus jujuba fruit. *Heliyon* [Internet]; **5**: e01768 (2019). Available from: https://www.sciencedirect.com/science/article/pii/S2405844019302348 doi: https://doi.org/10.1016/j.heliyon.2019.e01768
23. Liguori I, Russo G, Curcio F, Bulli G, Aran L, Della-Morte D, *et al*. Oxidative stress, aging, and diseases. *Clin Interv Aging;* **13**: 757–72 (2018). https://doi.org/10.2147/CIA.S158513
24. Zuo L, Prather ER, Stetskiv M, Garrison DE, Meade JR, Peace TI, *et al*. Inflammaging and Oxidative Stress in Human Diseases: From Molecular Mechanisms to Novel Treatments. *Int J Mol Sci* [Internet]; **20**(18):1–39. Available from: https://pubmed.ncbi.nlm.nih.gov/31510091/ doi: 10.3390/ijms20184472