

Anti-noncommunicable diseases attributes of pineapple (*Ananas comosus*): a concise review

¹Kumalawati, D.A., ^{1,*}Nurkolis, F., ²Wewengkang, D.S., ³Permatasari, H.K., ²Rotinsulu, H., ⁴Taslim, N.A., ⁵Joseph, V. and ⁶Samtiya, M.

¹Department of Biological Sciences, Faculty of Sciences and Technology, State Islamic University of Sunan Kalijaga, Yogyakarta, Indonesia

²Pharmacy Department of Sam Ratulangi University, Kampus Unsrat Bahu Street, Manado, Indonesia

³Department of Biochemistry and Biomolecular, Faculty of Medicine, Brawijaya University, Malang, Indonesia

⁴Clinical Nutrition, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia

⁵Cardiology Department, Faculty of Medicine, Sam Ratulangi University, Manado, Indonesia

⁶Department of Nutrition Biology, Central University of Haryana, Haryana 123031, India

Article history:

Received: 5 November 2021

Received in revised form: 6

December 2021

Accepted: 10 March 2022

Available Online: 19

November 2022

Abstract

Pineapple (*Ananas comosus*) is a tropical fruit that is numerous in Indonesia. This fruit can be processed into various processed food products. This author writes this article to find out the potential of pineapple as a food product that can be anti-noncommunicable diseases (NCDs) such as diabetes, obesity, oxidative stress, and cancer. This article is written using the narrative review method where data are collected from literature studies, namely articles in journals, books, and other literature-based online on database portals and leading search engines such as PUBMED and NCBI, the official website of the USDA (United States Department of Agriculture) and the European Phenols Explorer. The collected data are then analyzed, synthesized, discussed in the discussion, and general conclusions are drawn. The findings uncovered that pineapple contains polyphenols and antioxidant components, which are pretty high in concentration and could be useful as anti-NCDs. This fruit also has a proteolytic enzyme, bromelains, which is an immunomodulator against viral infections and diseases. This review concluded that pineapple fruit can be processed into various functional food products through several methods to maintain the content of polyphenols and antioxidants that have anti-NCDs potentials. It is necessary to process or execute this idea to identify and feel its benefits according to the research objectives, and *in vivo*, clinical trials are needed.

Keywords:

Pineapple,

Noncommunicable diseases,

Antioxidants,

Polyphenols,

Bromelains

DOI:

1. Introduction

The main problem of non-communicable diseases (NCDs) experienced in Indonesia is obesity. Obesity is a risk factor for all NCDs, such as coronary heart disease, cancer, and diabetes. WHO data in 2011 reported that some of the main factors that cause non-communicable diseases are unhealthy or poor lifestyles. One of the main unhealthy lifestyles is the pattern of consumption of foods that contain excess sugar or foods that taste sweet. Therefore, the government establishes the Healthy Living Community Movement (GERMAS) program. This program limits daily sugar intake to 50 grams per day. In addition, through this program, the government supports physical activity as an effort to avoid NCDs. However, due to the consumption habits of Indonesian people who always want to eat sweet foods because they

contain excess sugar (KemenKes, 2013), NCDs prevalence remains high in Indonesia.

Death caused by COVID-19 is related to comorbid factors, such as NCDs (Pal and Bhadada, 2020). As a developed country with a high prevalence of non-communicable diseases (NCDs) such as diabetes, coronary heart disease and obesity, America has a high probability factor for COVID-19 (Mavrogenis *et al.*, 2020). High-income or developed countries have a higher risk of experiencing COVID-19, showing that non-communicable diseases are spread worldwide and are significantly associated with increased mortality from the COVID-19 pandemic (McCloskey *et al.*, 2020). The prevalence of NCDs prevalence in Indonesia has increased by more than 34% (KemenKes, 2018).

*Corresponding author.

Email: fahrul.nurkolis.mail@gmail.com

Additionally, NCDs appear without symptoms and do not show specific clinical signs (disguised), so many people are unaware of the dangers of NCDs. Therefore, we need a breakthrough in the treatment of NCDs, a national and global problem, by replacing these food ingredients with functional foods made from natural ingredients from Indonesian local wisdom, rich in antioxidants and polyphenol content. Meta-analysis studies have shown that antioxidants and polyphenols can significantly improve lipid profiles and blood sugar fluctuations that affect anti-NCDs (Farhangi *et al.*, 2020; Ma and Chen, 2020; Rompies *et al.*, 2021; Permatasari *et al.*, 2021). A potential local fruit is pineapples, which have a sweet taste and are rich in antioxidants and polyphenols. However, this potential fruit has not been widely used for healthy food purposes (Hossain and Rahman, 2011). The authors want to do innovations and examine the potential of pineapples against non-communicable diseases to use them as anti-NCDs therapy.

2. Methodology

This article was written using the literature study method or literature study, the data obtained were sourced from NCBI (National Center for Biotechnology Information USA) with ("antioxidants" [All Fields] OR "antioxidants" [MeSH Terms] OR "antioxidants" [All Fields] OR "antioxidant" [All Fields]) AND ("polyphenols" [MeSH Terms] OR "polyphenols" [All Fields]) AND ("anas" [MeSH Terms] OR "anas" [All Fields] OR "pineapple" [All Fields])) AND ("2011/01/07" [PDat]: "2021/01/04" [PDat]) for the last five years from 07 January 2016 to 04 January 2021. Also related to non-communicable diseases, a literature study was conducted again with (("polyphenols" [MeSH Terms] OR "polyphenols" [All Fields]) AND non-communicable diseases [All Fields]) AND ("12/29/2010" [PDat]: "2020/12/25" [PDat]). Data related to prevalence and other data were obtained from the government's official website and the World Health Organization (WHO). The results obtained are then analyzed in the description in the Results and Discussion section of this article.

3. Results and discussion

3.1 Noncommunicable diseases

Noncommunicable diseases (NCDs) are health problems that have become a national and global concern. The WHO data for 2008 show that of the 57 million deaths that occurred, 36 million or nearly two-thirds were caused by non-communicable diseases. In countries with low to medium economic levels, NCDs have caused mortality in 29% of people aged less than 60

years (WHO, 2015). Based on data from the World Health Organization (WHO), 40.5 million of the 56.9 million people in the world died from noncommunicable diseases in 2016 (WHO, 2017). Data from the Ministry of Health of the Republic of Indonesia show that from 2013 to 2018, the prevalence of NCDs in Indonesia increased by more than 34% (KemenKes, 2018). The main problem of NCDs experienced in Indonesia is obesity, and obesity is a risk factor for all NCDs such as coronary heart disease, cancer, and diabetes. According to WHO data reported in 2011, some of the main factors that cause non-communicable diseases are unhealthy or poor lifestyles.

3.2 Food factor

Lifestyle is one of the critical factors affecting health because the wrong diet can reduce health and even trigger various degenerative diseases. Today, people pay special attention to degenerative diseases or non-communicable diseases (NCDs) and diabetes mellitus (WHO, 2016). One of the leading causes of diabetes is an unhealthy lifestyle, consuming foods containing excess sugar or foods with a sweet and persistent taste. Diabetes Mellitus (DM) is a group of metabolic syndrome diseases characterized by hyperglycaemic (high blood sugar levels) due to impaired insulin secretion or insulin action. Chronic hyperglycemic from diabetes is associated with long-term damage and impaired blood vessel function (Care, 2013). According to the World Health Organization (WHO) report, approximately 347 million people worldwide suffer from DM. Diabetes deaths are estimated to increase two-thirds of the time by 2030. The burden of diabetes is rising globally, especially in developing countries (WHO, 2016). Indonesia is the fourth largest DM sufferer worldwide, with a prevalence of 8.6% of the total population. According to Basic Health Research (KemenKes, 2013), there was an increase in the prevalence of DM sufferers, from 1.1% in 2007 to 1.5% in 2013 (KemenKes, 2013). People with DM must control glucose levels within the normal range to avoid complications.

3.3 Antioxidants and polyphenol content in pineapple

Based on the data collection results, several articles showed polyphenol levels in pineapple (*Ananas comosus*). The data is shown in Table 1.

Table 1 shows that Pineapple (*Ananas comosus*) contains several high concentrations of polyphenols, including gallic acid, larciresinol, matairesinol, medioresinol, pinoresinol, secoisolariciresinol and syringaresinol (Moniruzzaman *et al.*, 2013; Lu *et al.*, 2014; Ferreira *et al.*, 2016; Abeyhuriya *et al.*, 2020;

Table 1. Polyphenol Levels in Pineapple Fruit

Type of test	Polyphenol level	References
Total Phenolic	31.48 to 77.55 mg equivalent gallic acid (GAE)/100 g of FW	Lu <i>et al.</i> (2014)
Total Phenolic	226.29±1.18 mg gallic acid/kg	Moniruzzaman <i>et al.</i> (2013)
Total phenolic content	31.3±0.6 mg GAE/100 g FW	Abey Suriya <i>et al.</i> (2020)
Polyphenol Content	Lariciresinol 0.20 mg/100g FW; Matairesinol 0.16 mg/100g FW; Medioresinol 2.00e-03 mg/100g FW; Pinosesinol 0.30 mg/100g FW; Secoisolariciresinol 0.21 mg/100g FW; Syringaresinol 0.09 mg/100g FW	Phenol-Explorer Database for the Flavonoid Content of Selected Foods (Pineapple) Phenol-Explorer (2021)
Total polyphenols (juices)	35.80 mg/100 mL	Phenol-Explorer Database for the Flavonoid Content of Selected Foods (Pineapple) Phenol-Explorer (2021)
Phenolic Compounds	126.95±7.51 mg gallic acid/100 g	Ferreira <i>et al.</i> (2016)

Phenol-Explorer, 2021). Seeing the benefits of polyphenols as shown in Table 2, polyphenols are empirically proven to be anti-noncommunicable diseases such as diabetes, obesity, heart disease, cancer, hypertension, and other non-communicable diseases (Cheng *et al.*, 2017; Grosso *et al.*, 2017; Omodanisi *et al.*, 2017; Williamson, 2017; Castro-Barquero *et al.*, 2018; Koch, 2019). However, there is still little use for pineapple as a processed functional product for health benefits, especially in anti-NCDs. However, it should also be noted that polyphenols are compounds or substances that are volatile and easily oxidized at high temperatures (Li *et al.*, 2014). Therefore, its use as a functional food product by maintaining polyphenol levels for health benefits is necessary to have a good production technology process such as freeze-drying to maintain the content of volatile compounds (Pisano *et al.*, 2013).

The levels of polyphenols obtained from the processes of the study of the literature related to the antioxidant content in pineapple are shown in Table 3.

Table 3 shows that pineapple (*Ananas comosus*) has a high content of polyphenols and antioxidants. Vitamin C, often called ascorbic acid contained in pineapples, is 131% of the diet reference intake (RDI), according to data from the United States Department of Agriculture (USDA). Vitamin C is a compound considered an antioxidant due to its ability to fight free radicals and is proven by testing against DPPH (Padayatty and Levine, 2016). Furthermore, pineapple fruit, according to research (Ferreira *et al.*, 2016), has vitamin C levels of vitamin c as an antioxidant of 62.11±9.49 mg/100 g and antioxidant activity of 21.75±2.06%. Based on the data presented in Table 4, antioxidants also play an essential role in the health of the body, such as fighting free radicals, anti-inflammatory and anti-non-communicable

Table 2. Effects of Polyphenols on NCDs

Supplementation	NCDs Effects	References
Polyphenols	Protect against oxidative damage or anti-stress oxidative	Omodanisi <i>et al.</i> (2017)
Polyphenols	Prevention of chronic noncommunicable diseases, cancers, cardiovascular	Koch (2019)
Polyphenols	activating β -oxidation; a prebiotic effect for the gut microbiota; inducing satiety; stimulating energy expenditure by inducing thermogenesis in brown adipose tissue; modulating adipose tissue inhibiting adipocyte	Castro-Barquero <i>et al.</i> (2018)
Polyphenols	Lowers endothelial dysfunction, lowers blood pressure and cholesterol, regulates energy metabolism, reduces the risk of developing type 2	Williamson (2017)
Polyphenols	Decreased risk of type 2 diabetes	Grosso <i>et al.</i> (2017)
Polyphenols	Inhibits the development of hypertension, diabetes mellitus, hyperlipidemia, and obesity	Cheng <i>et al.</i> (2017)

Table 3. Antioxidant Levels in Pineapple Fruit

Type of test	Polyphenol level	References
Ascorbic acid	5.08 to 33.57 mg/100 g of fresh weight (FW)	Lu <i>et al.</i> (2014)
Total Vitamin C Contents (TVC)	31.2±2.4 mg/100 g FW	Abey Suriya <i>et al.</i> (2020)
Vitamin C	131% of the RDI	USDA Database for the Flavonoid Content of Selected Foods Pineapple)
Vitamin C	62.11±9.49 mg/100 g	Ferreira <i>et al.</i> (2016)
Antioxidant Activity	21.75±2.06% inhibition	Ferreira <i>et al.</i> (2016)

diseases such as oxidative stress, obesity, diabetes, and other NCDs. Therefore, based on the potential of pineapple fruit, which has high polyphenols and antioxidants such as vitamin C and the bromelains enzyme, this fruit could be used as a functional food that can be effective against anti-NCDs, which is still a high prevalence even in the world.

3.4 Polyphenols for anti-non-communicable diseases

Many studies revealed the benefits of polyphenols for health, one of which is anti-NCDs. Most polyphenols are found in vegetable and fruit foods; the data from a literature study shows the benefits of polyphenols as anti-NCDs in Table 2A.

3.5 Antioxidants for anti-non-communicable diseases

Not only polyphenols that can be anti-NCDs but empirically, antioxidants, especially ascorbic acid, can also be an alternative in the treatment of NCDs. The following are the results of the literature study obtained and presented in Table 4.

3.6 Bromelains for anti-non-communicable diseases

Bromelains is a protein-digesting enzyme found in pineapple (*Ananas comosus*) and has health benefits such as anti-inflammatory, anticancer, and anti-cardiovascular disease (Pavan *et al.*, 2012). In addition to being anti-NCDs, recent research has exposed that pineapple bromelains can be an alternative immunomodulatory and anti-COVID-19 (Sagar *et al.*, 2020; Yanuck *et al.*, 2020). Furthermore, currently available meta-analysis studies have shown that bromelains have a beneficial effect in reducing pain and positively impacting postoperative third-molar patients (Mendes *et al.*, 2019).

Pineapple (*Ananas comosus*) has many benefits because it sees polyphenols, antioxidants (Vitamin C or ascorbic acid), and the digestive enzyme Bromelains (Figure 1). Several studies have shown that even meta-analysis of polyphenols and antioxidants has become a trend in the field of nutrition and food to improve the

nutritional status of the global community, such as minimizing the incidence of non-communicable diseases, including diabetes, obesity, oxidative stress or chronic inflammation, cancer, hypertension, heart disease, and other NCDs. Thus, now there is a need for an innovation that can be commercialized and will have a massive impact on the control and eradication of NCDs in Indonesia and even around the world by processing pineapple fruit into functional foods rich in antioxidants and polyphenols, which are not only anti-NCDs but also have immunomodulatory potential against viral infections such as COVID-19. Therefore, it is necessary to execute the idea, and its output will be copyrighted or patented.

Anti-Noncommunicable Diseases Attributes of Pineapple (*Ananas comosus*)

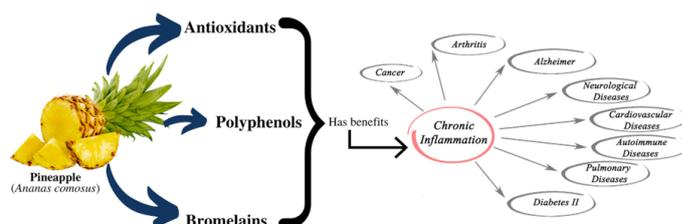


Figure 1. Benefits of Pineapple (*Ananas comosus*) in non-communicable diseases

4. Conclusion

Pineapple (*Ananas comosus*) is a fruit high in antioxidants, polyphenols, and bioactive peptides (bromelains), which can be an alternative to noncommunicable anti-cancer diseases. Additionally, further studies in experimental animals and clinical trials in humans need to support this review.

Conflicts of interest

All researchers declare no conflict of interest and permit to reproduce material from other sources. This research was financed by the author only (Personal Funding). There are no underlying data related to this paper. This is a concise narrative review, not a systematic review, so it does not require reporting

Table 4. Antioxidant Effects on NCDs

Supplementation	NCDs Effects	References
Vitamin C (systematic review)	Reduce the all-cause risk of death from noncommunicable	Jayedi <i>et al.</i> (2018)
Total antioxidant capacity of	It was related to a lower risk of type 2 diabetes	van der Schaft <i>et al.</i> (2019)
Vitamin C	Down-regulating NADPH oxidase suppresses NF- κ B activation and prevents oxidation of tetrahydro-biopterin - a cofactor of NO synthase - lowers the risk of heart disease	Tibaut and Petrovi (2016)
Vitamin C	Improve lipid profiles (HDL, LDL, TGL), insulin, and	Pearson <i>et al.</i> (2017)
Ascorbic Acid	Significant anti-inflammatory effect by lowering levels of inflammatory factors such as TNF- α , SAA, and hs-CRP in	Jamalan <i>et al.</i> (2015)

guidelines.

Acknowledgements

I express my gratitude to Prof. Ir. Hardinsyah, MS., PhD (as President of the Federations of Asian Nutrition Societies; President of the Food and Nutrition Society of Indonesia; and Chair of the Southeast Asia Probiotics Scientific and Regulatory Experts Network), and Prof. Dr. Nurpudji A Taslim, MD, MPH, Sp.GK (K) (Chair of the Indonesian Clinical Nutrition Physician Association), who has provided comments, suggestions, and input in the research and writing of this article, as well as motivation to keep the passion for research during the pandemic.

References

- Abesuriya, H.I., Bulugahapitiya, V.P. and Loku Pulukkuttige, J. (2020). Total vitamin C, ascorbic acid, dehydroascorbic acid, antioxidant properties, and iron content of fruits underutilized and commonly consumed in Sri Lanka. *International Journal of Food Science*, 2020, 4783029. <https://doi.org/10.1155/2020/4783029>.
- Care, A.D. (2013). Standards of Medical Care in Diabetes 2013. *American Diabetes Association*, 36 (Supplement 1), S11-S66. <https://doi.org/10.2337/dc13-S011>.
- Castro-Barquero, S., Lamuela-Raventós, R.M., Doménech, M. and Estruch, R. (2018). Relationship between Mediterranean dietary polyphenol intake and obesity. *Nutrients*, 10(10), 1523. <https://doi.org/10.3390/nu10101523>
- Cheng, Y.C., Sheen, J.M., Hu, W.L. and Hung, Y.C. (2017). Polyphenols and Oxidative Stress in Atherosclerosis-Related Ischemic Heart Disease and Stroke. *Oxidative Medicine and Cellular Longevity*, 2017, 8526438. <https://doi.org/10.1155/2017/8526438>
- Farhangi, M.A., Vajdi, M. and Fathollahi, P. (2020). Dietary total antioxidant capacity (TAC), general and central obesity indices and serum lipids among adults: An updated systematic review and meta-analysis. *International Journal for Vitamin and Nutrition Research*, 92(5-6), a000675. <https://doi.org/10.1024/0300-9831/a000675>.
- Ferreira, E.A., Siqueira, H.E., Boas, E.V.V., Hermes, V.S. and Rios, A.D.O. (2016). Bioactive Compounds and Antioxidant Activity of Pineapple Fruit of Different Cultivars. *Revista Brasileira de Fruticultura*, 38, e-146. <https://doi.org/10.1590/0100-29452016146>.
- Grosso, G., Stepaniak, U., Micek, A., Kozela, M., Stefler, D., Bobak, M. and Pajak, A. (2017). Dietary polyphenol intake and risk of type 2 diabetes in the Polish arm of the Health, Alcohol and Psychosocial factors in Eastern Europe (HAPIEE) study. *British Journal of Nutrition*, 118(1), 60- 68. <https://doi.org/10.1017/S0007114517001805>.
- Hossain, M.A. and Rahman, S.M.M. (2011). Total phenolics, flavonoids and antioxidant activity of tropical fruit pineapple. *Food Research International*, 44(3), 672-676. <https://doi.org/10.1016/j.foodres.2010.11.036>.
- Jamalan, M., Rezazadeh, M., Zeinali, M. and Ghaffari, M.A. (2015). Effect of ascorbic acid and alpha-tocopherol supplementations on serum leptin, tumor necrosis factor alpha, and serum amyloid A levels in individuals with type 2 diabetes mellitus. *Avicenna Journal of Phytomedicine*, 5(6), 531-539. <https://doi.org/10.22038/ajp.2015.4453>.
- Jayedi, A., Rashidy-Pour, A., Parohan, M., Zargar, M.S. and Shab-Bidar, S. (2018). Dietary antioxidants, circulating antioxidant concentrations, total antioxidant capacity, and risk of all cause mortality: A systematic review and dose-response meta-analysis of prospective observational studies. *Advances in Nutrition*, 9(6), 701-716. <https://doi.org/10.1093/advances/nmy040>
- KemenKes, R.I. (2013). Riset kesehatan dasar (Riskesdas) 2013. Jakarta, Indonesia: Badan Penelitian dan Pengembangan Kesehatan Kementerian Kesehatan Republik Indonesia. [In Bahasa Indonesia].
- KemenKes, R.I. (2018). HASIL UTAMA RISKESDAS 2018 Kementerian. Retrieved from website: <http://www.depkes.go.id/resources/download/info-terkini/hasil-riskesdas-2018.pdf>. [In Bahasa Indonesia].
- Koch, W. (2019). Dietary polyphenols-important non-nutrients in the prevention of chronic non-communicable diseases. A systematic review. *Nutrients*, 11(5), 1039. <https://doi.org/10.3390/nu11051039>.
- Li, A.N., Li, S., Zhang, Y.J., Xu, X.R., Chen, Y.M. and Li, H.B. (2014). Resources and biological activities of natural polyphenols. *Nutrients*, 6(12), 6020-6047. <https://doi.org/10.3390/nu6126020>.
- Lu, X.H., Sun, D.Q., Wu, Q.S., Liu, S.H. and Sun, G.M. (2014). Physico-chemical properties, antioxidant activity and mineral contents of pineapple genotypes grown in China. *Molecules*, 19 (6), 8518-8532. <https://doi.org/10.3390/molecules19068518>.
- Ma, G. and Chen, Y. (2020). Polyphenol supplementation benefits human health via gut

- microbiota: A systematic review via meta-analysis. *Journal of Functional Foods*, 66, 103829. <https://doi.org/10.1016/j.jff.2020.103829>.
- Mavrogenis, A.F., Quaile, A. and Scarlat, M.M. (2020). The virus crisis affects Orthopaedic surgery and scientific activities worldwide. *International Orthopaedics*, 44(5), 813-817. <https://doi.org/10.1007/s00264-020-04557-2>.
- McCloskey, E.V., Harvey, N.C., Johansson, H., Lorentzon, M., Vandenput, L., Liu, E. and Kanis, J.A. (2020). Global impact of COVID-19 on non-communicable disease management: descriptive analysis of access to FRAX fracture risk online tool for prevention of osteoporotic fractures. *Osteoporosis International*, 32(1), 39-46. <https://doi.org/10.1007/s00198-020-05542-6>
- Mendes, M.L.T., DoNascimento-Júnior, E.M., Reinheimer, D.M. and Martins-Filho, P.R.S. (2019). Efficacy of proteolytic enzyme bromelain on health outcomes after third molar surgery. Systematic review and meta-analysis of randomized clinical trials. *Medicina Oral Patologia Oral y Cirugia Bucal*, 4(1), e61–e69. <https://doi.org/10.4317/medoral.22731>.
- Moniruzzaman, M., Khalil, M.I., Sulaiman, S.A. and Gan, S.H. (2013). Physicochemical and antioxidant properties of Malaysian honeys produced by *Apis cerana*, *Apis dorsata* and *Apis mellifera*. *BMC Complementary and Alternative Medicine*, 13, 43. <https://doi.org/10.1186/1472-6882-13-43>.
- Omodanisi, E.I., Aboua, Y.G., Oguntibeju, O.O. and Lamuela-Raventós, R.M. (2017). Assessment of the anti-hyperglycaemic, anti-inflammatory and antioxidant activities of the methanol extract of *Moringa oleifera* in diabetes-induced nephrotoxic male wistar rats. *Molecules*, 22(4), 439. <https://doi.org/10.3390/molecules22040439>.
- Padayatty, S.J. and Levine, M. (2016). Vitamin C: the known and the unknown and Goldilocks. *Oral Diseases*, 22(6), 463–493. <https://doi.org/10.1111/odi.12446>.
- Pal, R. and Bhadada, S.K. (2020). COVID-19 and non-communicable diseases. *Postgraduate Medical Journal*, 96, 429–430. <https://doi.org/10.1136/postgradmedj-2020-137742>.
- Pavan, R., Jain, S., Shraddha. and Kumar, A. (2012). Properties and Therapeutic Application of Bromelain: A Review. *Biotechnology Research International*, 2012, 976203. <https://doi.org/10.1155/2012/976203>.
- Pearson, J.F., Pullar, J.M., Wilson, R., Spittlehouse, J.K., Vissers, M.C.M., Skidmore, P.M.L., Willis, J., Cameron, V.A. and Carr, A.C. (2017). Vitamin C status correlates with markers of metabolic and cognitive health in 50-year-olds: Findings of the CHALICE cohort study. *Nutrients*, 9(8), 831. <https://doi.org/10.3390/nu9080831>.
- Permatasari, H.K., Nurkolis, F., Augusta, P.S., Mayulu, N., Kuswari, M., Taslim, N.A., Wewengkang, D.S., Batubara, S.C. and Gunawan, W.B. (2021). Kombucha tea from seagrapes (*Caulerpa racemosa*) potential as a functional anti-ageing food: *in vitro* and *in vivo* study. *Heliyon*, 7(9), e07944. <https://doi.org/10.1016/j.heliyon.2021.e07944>
- Phenol-Explorer. (2021). Database on polyphenol content in foods. Version 3.6. Retrieved January 4, 2021 from Phenol-Explorer website: <http://phenol-explorer.eu/contents/food/161>.
- Pisano, R., Fissore, D., Barresi, A.A. and Rastelli, M. (2013). Quality by design: Scale-up of freeze drying cycles in pharmaceutical industry. *AAPS PharmSciTech*, 14(3), 1137–1149. <https://doi.org/10.1208/s12249-013-0003-9>.
- Rompies, R., Mayulu, N., Nurkolis, F., Faradila, F., Kepel, B.J. and Natanael, H. (2021). Antioxidant capacity of snack cookies made from mango and pineapple fermentation. *Food Research*, 5(5), 145-148. [https://doi.org/10.26656/fr.2017.5\(5\).010](https://doi.org/10.26656/fr.2017.5(5).010)
- Sagar, S., Rathinavel, A.K., Lutz, W.E., Struble, L.R., Khurana, S., Schnaubelt, A.T., Mishra, N.K., Guda, C., Broadhurst, M.J., Reid, S.P.M., Bayles, K.W., Borgstahl, G.E.O. and Radhakrishnan, P. (2020). Bromelain Inhibits SARS-CoV-2 Infection in VeroE6 Cells. *BioRxiv*, 2020, 297366. <https://doi.org/10.1101/2020.09.16.297366>.
- Tibaut, M. and Petrovi, D. (2016). Oxidative Stress Genes, Antioxidants and Coronary Artery Disease in Type 2 Diabetes Mellitus. *Cardiovascular and Hematological Agents in Medicinal Chemistry*, 14 (1), 23–38. <https://doi.org/10.2174/1871525714666160407143416>.
- Van der Schaft, N., Schoufour, J.D., Nano, J., Kieftede Jong, J.C., Muka, T., Sijbrands, E.J.G., Ikram, M.A., Franco, O.H. and Voortman, T. (2019). Dietary antioxidant capacity and risk of type 2 diabetes mellitus, prediabetes and insulin resistance: the Rotterdam Study. *European Journal of Epidemiology*, 34(9), 853–861. <https://doi.org/10.1007/s10654-019-00548-9>.
- Williamson, G. (2017). The role of polyphenols in modern nutrition. *Nutrition Bulletin*, 42(3), 226-235. <https://doi.org/10.1111/nbu.12278>.
- World Health Organization (WHO). (2016). GLOBAL REPORT ON DIABETES WHO Library

- Cataloguing-in-Publication Data Global report on diabetes. Retrieved from WHO website: http://www.who.int/about/licensing/copyright_form/index.html.
- World Health Organization (WHO). (2015). World Health Statistics 2015. Retrieved from WHO website: <https://www.who.int/docs/default-source/gho-documents/world-health-statistic-reports/world-health-statistics-2015.pdf>
- World Health Organization (WHO). (2017). Noncommunicable diseases progress monitor. Retrieved from WHO website: <https://www.who.int/publications-detail-redirect/9789241513029>
- Yanuck, S.F., Pizzorno, J., Messier, H. and Fitzgerald, K.N. (2020). Evidence Supporting a Phased Immuno-physiological Approach to COVID-19 From Prevention Through Recovery. *Integrative Medicine*, 19(Suppl. 1), 8–35. <http://www.ncbi.nlm.nih.gov/pubmed/32425712>