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More *Ulam* for Your Brain: A Review on the Potential Role of *Ulam* in Protecting Against Cognitive Decline

(Lebihkan Ulam untuk Otak Anda: Suatu Kajian tentang Potensi Ulam dalam Lindungi Penyusutan Fungsi Kognitif)

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ABSTRACT

Ulam *is the South East Asian traditional vegetables which contains high total phenolic content and exhibits antioxidant activity. Several studies have reported the potential of neuroprotective effect of* ulam. *The objective of this review article was to highlight the total phenolic content (TPC) and antioxidant activity of* ulam *and the roles of phenolic content that can contribute to attenuation of cognitive decline. The review includes randomized controlled trial and experimental studies from year 2007 to 2017. In this review, PRISMA method was used to report the results (*n*=15). Phenolic compounds, ie plants' second metabolites of selected* ulam *in South East Asia were also discussed in this review, with respect to its potential for health promotion which and reducing the risk of cognitive disease.* Oenanthe javanica (selom)*,* Ocimum basilicum (daun selasih) *and* Anacardium occidentale *L.* (pucuk gajus) *were ranked in the top three highest TPC among all the selected* ulam. *In general,* Polygonum minus (kesum)*,* Anacardium occidentale *L.* (pucuk gajus) *and* Cosmos caudatus (ulam raja) *exhibited high DPPH radical scavenging activity whereas* Anacardium occidentale *L.* (pucuk gajus) *exhibited highest ferric ion reducing potential (FRAP) among all the selected* ulam *in South East Asia countries. Overall, some studies had shown* Centella asiatica (pegaga), Oenanthe javanica (selom), Polygonum minus (kesum), Ocimum basilicum (daun selasih) *and* Murraya koenigii (daun kari) *are beneficial in improving cognitive status and mood. The bioactive compounds in* ulam *may exhibit neuroprotective effects but human studies are still lacking in exploring the relationship between* ulam *consumption and cognitive status.*

Keywords: Antioxidant; cognitive; mood; phenolic; ulam

ABSTRAK

*Ulam merupakan sayuran tradisi Asia Tenggara yang mengandungi kandungan fenolik yang tinggi dan menunjukkan aktiviti antioksidan. Beberapa kajian melaporkan ulam berpotensi sebagai pelindung neuro. Objektif kertas ini adalah untuk membandingkan jumlah kandungan fenolik (TPC), aktiviti antioksidan ulam serta peranan kandungan fenolik yang mengelakkan penyusutan fungsi kognitif. Ulasan kertas ini meliputi ujian klinikal dan uji kaji dari tahun 2007 hingga 2017. Dalam ulasan ini, kaedah PRISMA digunakan untuk melaporkan keputusan (*n*=15). Sebatian fenolik, i.e. metabolit sekunder tumbuhan daripada beberapa ulam terpilih di Asia Tenggara juga dibincangkan dalam ulasan ini daripada segi potensinya dalam mempromosikan kesihatan dan mengelakkan penyusutan fungsi kognitif.* Oenanthe javanica *(selom),* Ocimum basilicum *(daun selasih) dan* Anacardium occidentale *L. (pucuk gajus) merupakan tiga TPC yang tertinggi dalam kalangan semua ulam terpilih. Secara umum,* Polygonum minus *(kesum),* Anacardium occidentale *L. (pucuk gajus) dan* Cosmos caudatus *(ulam raja) menunjukkan aktiviti pemotongan radikal DPPH yang tinggi manakala* Anacardium occidentale *L. (pucuk gajus) menunjukkan potensi penurunan ion ferik tertinggi dalam kalangan semua ulam yang terpilih di negara-negara Asia Tenggara. Secara keseluruhan, beberapa kajian telah menunjukkan* Centella asiatica *(pegaga),* Oenanthe javanica *(selom),* Polygonum minus *(kesum),* Ocimum basilicum *(daun selasih) dan* Murraya koenigii *(daun kari) bermanfaat dalam meningkatkan fungsi kognitif dan emosi. Sebatian bioaktif dalam ulam berpotensi memberi kesan sebagai pelindung neuro namun kajian manusia yang menerokai hubungan antara pengambilan ulam dengan status kognitif masih terhad.*

Kata kunci: Antioksidan; emosi; fenolik; kognitif; ulam

INTRODUCTION

Ulam is the traditional vegetables which are normally consumed in a raw form among South East Asian populations such as in Indonesia, Thailand and Malaysia. It is usually eaten together with rice-based meal or a blend of fermented sauces, such as *budu*, *cincalok* or *sambal* (Huda-Faujan et al. 2007; Reihani & Azhar 2012). Within Asian countries, more than 120 species of *ulam* have been discovered and they are rich in carbohydrates, proteins, minerals and vitamins (Mohd Shukri et al. 2011). *Ulam* or traditional vegetables which commonly consumed by the South East Asian populations are listed in Table 1.

TABLE 1. List of selected *ulam* in South East Asia

Scientific name	Local name
Anacardium occidentale L.	*Pucuk gajus/ Yot-mamuang- himmaphan*
Centella asiatica	*Pegaga/ Gotu Kola/Antanan*
Cosmos caudatus	*Ulam raja/kenikir*
Kaempferia galanga L.	*Cekur*
Mentha arvensis L.	*Daun pudina*
Morinda elliptica	*Mengkudu*
Murraya koenigii	*Daun kari*
Ocimum basilicum	*Daun selasih*
Ocimum americanum	*Kemangi*
Oenanthe javanica	*Selom/Pak-Chilom*
Parkia speciosa	*Petai*
Plucea indica (L.)	*Beluntas*
Polygonum minus	*Kesum*

On average, Malaysian adults consumed 40 g/person/day of *ulam* (Nurul Izzah et al. 2012). Many studies among animal and human have reported that *ulam* exhibit various medicinal properties, such as antidiabetic, antihypertensive, neuroprotective and anti-inflammatory (Amalia et al. 2012; Bachok et al. 2014). The consumption of *ulam* has been promoted in key message 5 in the Malaysian Dietary Guidelines 2010 (National Coordinating Committee on Food and Nutrition. Ministry of Health Malaysia 2010) as *ulam* tends to increase the serum of Vitamin C, E, folic acid, β-carotene and lycopene. It has also been reported to be rich in polyphenols (Su & Arab 2006) that may be beneficial in improving cognitive status (Rosli et al. 2014). Medicinal plants such as herbs and *ulam* are therapeutic agents which have been used in many cultures but studies regarding the development of *ulam* as fortified food products are still limited.

Mild-cognitive impairment (MCI) is the intermediate stage between healthy aging and dementia (Petersen et al. 2014). Individuals with MCI have been identified to be at a higher risk of developing dementia after a few years (Burns & Zaudig 2002). A study has estimated that dementia and Alzheimer's disease in the world will be doubled for every 20 years and reach 81 million by 2040 (Reitz et al. 2011)and is predicted to double every 20 years through to 2040, leading to a costly burden of disease. Alzheimer disease (AD. Specifically in South East Asia there were approximately 2.48 million dementia patients in 2010 and the number is estimated to increase to 11.13 million in 2050 (Prince et al. 2013). According to the National Health Morbidity Survey, the prevalence of poor mental health among Malaysian aged above 16 years old ranged from 19.6% to 34.7% (Institute for Public Health 2015). The prevalence of mild cognitive impairment in Malaysia's elderly population was 16% (Vanoh et al. 2017). Previous studies have reported the favorable effect such as *Polygonum minus* supplementation has improved both attention and memory among middle aged women (Shahar et al. 2015). Furthermore, *Ginkgo biloba* and *Centella asiatica* have improved cognitive impairment related with aging and other disorders such as Alzheimer and dementia (Gambhir 2008; Solomon et al. 2002). However, such benefits of *ulam* are yet to be reviewed systematically for its neuroprotective effect among South East Asian populations.

METHODS

The search for published research papers that related to *ulam* consumption and cognitive status were conducted on PUBMED, Science Direct, Scopus, Springer and Google Scholar databases for articles published from 2007 to 2017 by using PRISMA method (Fokkens et al. 2005). The review includes randomized controlled trial and experimental studies. The keywords that were used in the database machine comprises of *ulam* consumption, total phenolic content, antioxidant activity and cognitive function among animal, adult and elderly population. A total of 138 records were identified through database searching, 123 records were excluded due to irrelevant content, *ulam* was not found in South East Asia countries and duplicate studies. Thus, a total of 15 studies were included in this review article (Figure 1). Local journals and unpublished theses were hand searched. Since the study is a review article, ethics approval is not required.

RESULT

PHENOLIC CONTENT AND ANTIOXIDANT ACTIVITY OF SELECTED *ULAM*

Total phenolic content of selected ulam Out of seven studies concerning total phenolic content and antioxidant activity of selected *ulam* in South East Asia, five studies were conducted in Malaysia and one study each conducted in Thailand and Indonesia, respectively (Table 2). Phenolic compounds are plants' secondary metabolite which have the potential in promoting health and possessed medical benefits (Mohd Akhtar et al. 2011). Phenolic compounds contribute as an antioxidant by scavenging the superoxide anion, hydroxy radical, peroxy radical and inhibiting lipid peroxidation in the biological system (Izunya et al.

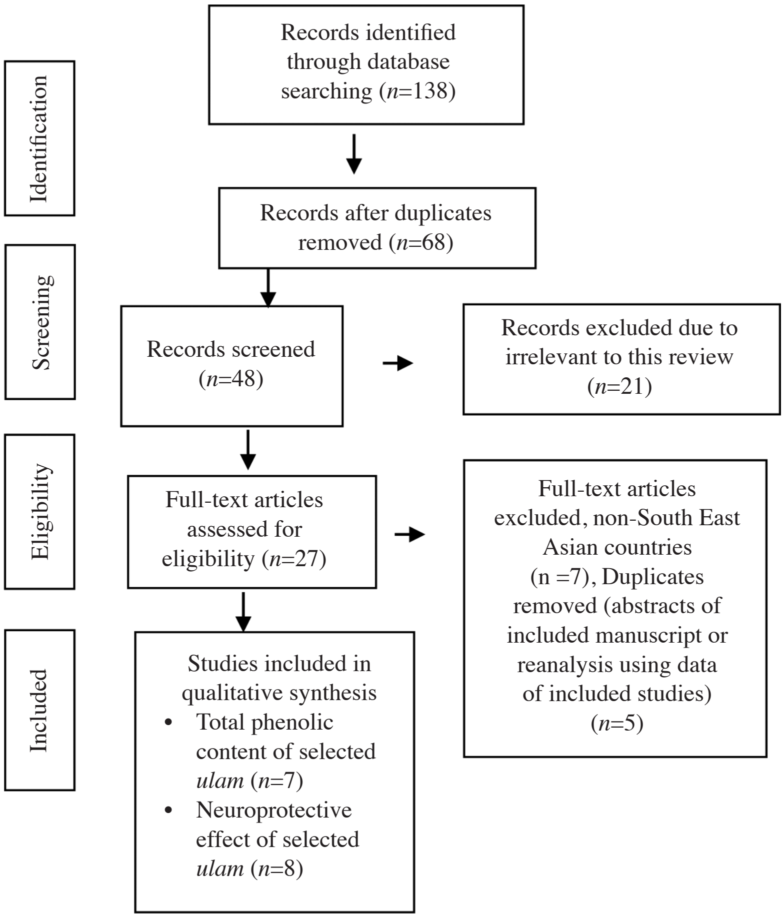

FIGURE 1. Review article flowchart

2010). Nowadays, consumers are concerned about the safety of the synthetic antioxidants products in market and looking for the natural products. Thus, many studies have been carried out to identify the safe and edible plants as supplements to overcome the health issues (Maizura et al. 2011). All the studies reviewed have used Folin-Ciocalteau method to analyze the TPC. The study by Nooraini et al. (2015) has determined TPC of *kesum, pegaga* and *ulam raja* extracts. For the pure extracts, the highest TPC was *kesum* (1388.19 ± 111 mgGAE/100 g), followed by *ulam raja* (323.59 ± 7.19 mgGAE/100 g) and *pegaga* (150.01 ± 37.93 mgGAE/100 g).

Another study in Malaysia by Reihani and Azhar (2012) has summarized the TPC of selected *ulams* in the following order: *daun kari*, *selom*, *ulam raja*, *pegaga* and *petai*. The extraction method used was 0.5 g of powdered sample added with 25 mL of deionized water. In another study, 1 g of powdered sample extracted with 50 mL methanol was used to analyze the TPC of selected *ulam* and ranked in the following order: *pucuk gajus*, *kesum*, *ulam raja*, *selom* and *pegaga* (Chiang Chan et al. 2014). Another study has used four different extraction methods to analyze the TPC of *ulam*, namely extraction in 70% acetone, 70% ethanol, 70% methanol and distilled water (Sulaiman et al. 2011). A study in Thailand reported the TPC of *Anacardium occidentale* L. as 4075.79 ± 54.24 mg GAE/100 g (Kongkachuichai et al. 2015). In Indonesia, the TPC of selected *ulams* can be ranked in the following order: *Cosmos caudatus*, *Centella asiatica* and *Plucea indica* L. (Andarwulan et al. 2010). Apparently, there was a variation in TPC of selected *ulam* among these different extraction methods. In general, *selom*, *daun selasih* and *pucuk gajus* were top 3 highest TPC despite the different methods of extraction.

DPPH free radical scavenging activity of selected ulam

DPPH (1,1-diphenyl-2-picrylhydrazyl) radical-scavenging activity was performed to analyze the antioxidant activity of selected *ulams* in South East Asia (Brand-Williams et al. 1995; Mavundza et al. 2010). The assay was based on the reduction of DPPH radicals which causes an absorbance drop at 515 nm of spectrophotometer. All samples were analyzed in triplicates and average of the results was reported. The antioxidant capacity was expressed as μmol Trolox equivalent or mg Gallic acid equivalent (Wong et al. 2006).

Reihani and Azhar (2012) study reported that *ulam raja* showed the highest antioxidant capacity followed by *selom*, *daun kari*, *petai* and *pegaga*. *Daun kari* has been identified to have the highest TPC but it has a relatively low antioxidant activity, probably due to poor specificity of the total phenolic assay (Escarpa & González 2001; Singleton

TABLE 2. Total phenolic content and antioxidant of selected *ulam* in South East Asia

Author	Title	Location	Extraction	Total polyphenol content / Antioxidant activity	Method	Results (unit)
(Reihani & Azhar 2012)	Antioxidant activity and total phenolic content in aqueous extracts of selected traditional Malay salads (*ulam*)	Kedah, Pulau Pinang, Malaysia	0.5 g of powdered sample with 25 mL of deionized water	Total phenolic content	Folin-Ciocalteau method	*Daun kari*: 33.2 (mg GAE/ g) *Selom*: 31.8 (mg GAE/ g) *Ulam Raja*: 31.3 (mg GAE/g) *Pegaga*: 11.2 (mg GAE/g) *Petai*: 6.5 (mg GAE/g)
				DPPH free radical scavenging activity	(Brand-Williams et al. 1995)	*Ulam Raja*: 212.8 (µmol TE/ g) *Selom* :185.9 (µmol TE/ g) *Daun kari*: 82.1 (µmol TE/ g) *Petai*: 67.6 (µmol TE/ g) *Pegaga*: 32.4 (µmol TE/ g)
				Ferric reducing antioxidant potential	(Benzie & Strain 1996)	*Selom*: 199.9 (µmol TE/ g) *Ulam Raja*: 183.1 (µmol TE/ g) *Daun kari*: 108.3 (µmol TE/ g) *Pegaga*: 66 (µmol TE/ g) *Petai*: 44.7 (vmol TE/ g)
(Sulaiman et al. 2011)	Effect of solvents in extracting polyphenols and antioxidants of selected raw vegetables	USM, Pulau Pinang, Malaysia	70% acetone	Total phenolic content	Folin-Ciocalteau method	*Pegaga*: 22.4 ± 2.1 (mg GAE/g) *Ulam raja*: 17.2 ± 1.0 (mg GAE/g) *Selom*: 46.2 ± 3.8 (mg GAE/g) *Pucuk gajus*: 29.2 ± 2.4 (mg GAE/g) *Daun kari*: 18.3 ± 1.7 (mg GAE/g) *Cekur*: 0.9 ± 0.1 (mg GAE/g) *Mengkudu:* 4.8 ± 0.5 (mg GAE/g) *Selasih*: 45.2 ± 3.5 (mg GAE/g) *Pudina*: 95.7 ± 5.1 (mg GAE/g)
				DPPH free radical scavenging activity	(Brand-Williams et al. 1995)	*Pegaga*: 4.0 ± 1.3 (mg GAE/g) *Ulam raja*: 19.4 ± 1.3 (mg GAE/g) *Selom*: 23.1 ± 7.2 (mg/GAE/g) *Pucuk gajus*: 15.4 ± 0.9 (mg GAE/g) *Daun kari*: 9.2 ± 1.2 (mg GAE/g) *Cekur:* 1.1 ± 0.0 (mg GAE/g) *Mengkudu:* 7.2 ± 1.5 (mg GAE/g) *Selasih*: 14.5 ± 2.5 (mg GAE/g) *Pudina*: 25.5 ± 7.3 (mg GAE/g)
				Ferric reducing antioxidant potential	(Firuzi et al. 2005)	*Pegaga*: 6.3 ± 0.5 (mg GAE/g) *Ulam raja*: 12.6 ± 5.9 (mg GAE/g) *Selom*: 3.7 ± 0.3 (mg/GAE/g) *Pucuk gajus*: 54.2 ± 1.5 (mg GAE/g) *Daun kari:* 7.9 ± 1.1 (mg GAE/g)

Continues TABLE 2.

Author	Title	Location	Extraction	Total polyphenol content / Antioxidant activity	Method	Results (unit)
						Cekur: 2.7 ± 0.2 (mg GAE/g) *Mengkudu*: 1.5 ± 0.1 (mg GAE/g) *Selasih*: 27.7 ± 2.0 (mg GAE/g) *Pudina*: 70.1 ± 0.6 (mg GAE/g)
				Total phenolic content	Folin-Ciocalteau method	*Pegaga*: 52.5 ± 0.7 (mg GAE/g) *Ulam raja*: 48.8 ± 2.0 (mg GAE/g) *Selom:* 42.1 ± 1.0 (mg GAE/g) *Pucuk gajus*: 43.6 ± 1.4 (mg GAE/g) *Daun kari*: 9.2 ± 0.7 (mg GAE/g) *Cekur*: 2.6 ± 0.5 (mg GAE/g) *Mengkudu*: 2.2 ± 0.3 (mg GAE/g) *Selasih*: 3.8 ± 0.6 (mg GAE/g) *Pudina*: 5.7 ± 1.4 (mg GAE/g)
				DPPH free radical scavenging activity	(Brand-Williams et al. 1995)	*Pegaga*: 5.1 ± 2.1 (mg GAE/g) *Ulam raja*: 19.6 ± 1.8 (mg GAE/g) *Selom*: 10.7 ± 1.3 (mg/GAE/g) *Pucuk gajus*: 13.1 ± 0.1 (mg GAE/g) *Daun kari*: 10.2 ± 0.6 (mg GAE/g) *Cekur*: 0.7 ± 0.0 (mg GAE/g) *Mengkudu*: 4.0 ± 0.6 (mg GAE/g) *Selasih*: 15.8 ± 0.1 (mg GAE/g) *Pudina:* 18.5 ± 1.7 (mg GAE/g)
				Ferric reducing antioxidant potential	(Firuzi et al. 2005)	*Pegaga:* 12.7 ± 0.1 (mg GAE/g) *Ulam raja*: 13.9 ± 4.7 (mg GAE/g) *Selom*: 3.6 ± 0.3 (mg/GAE/g) *Pucuk gajus*: 43.4 ± 4.2 (mg GAE/g) *Daun kari:* 5.8 ± 0.2 (mg GAE/g) *Cekur*: 0.9 ± 0.0 (mg GAE/g) *Mengkudu*: 1.0 ± 0.1 (mg/GAE/g) *Selasih*: 15.6 ± 0.1 (mg/GAE/g) *Pudina*: 2.8 ± 0.1 (mg/GAE/g)
			70% methanol	Total phenolic content	Folin-Ciocalteau method	*Pegaga*: 1.4 ± 0.7 (mg GAE/g) *Ulam raja*: 1.7 ± 0.8 (mg GAE/g) *Selom*: 25.4 ± 3.7 (mg GAE/g) *Pucuk gajus*: 44.8 ± 1.8 (mg/GAE/g) *Daun kari*: 11.1 ± 0.3 (mg/GAE/g) *Cekur*: 2.0 ± 0.4 (mg/GAE/g) *Mengkudu*: 1.7 ± 0.1 (mg/GAE/g) *Selasih*: 10.8 ± 0.3 (mg/GAE/g) *Pudina*: 6.1 ± 1.2 (mg/GAE/g)

Continues TABLE 2.

Author	Title	Location	Extraction	Total polyphenol content / Antioxidant activity	Method	Results (unit)
				DPPH free radical scavenging activity	(Brand-Williams et al. 1995)	*Pegaga:* 8.1 ± 0.2 (mg GAE/g) *Ulam raja*: 23.2 ± 1.0 (mg GAE/g) *Pegaga*: 0.7 ± 0.0 (mg GAE/g) *Ulam raja*: 11.0 ± 3.6 (mg GAE/g) *Selom*: 40.4 ± 2.6 (mg/GAE/g) *Pucuk gajus*:16.2 ± 1.2 (mg/GAE/g) *Daun kari*: 7.0 ± 0.3 (mg/GAE/g) *Cekur*: 0.8 ± 0.1 (mg/GAE/g) *Mengkudu*: 0.7 ± 0.0 (mg/GAE/g) *Selasih*: 17.5 ± 0.2 (mg/GAE/g) *Pudina*: 21.1 ± 1.3 (mg/GAE/g)
				Ferric reducing antioxidant potential	(Firuzi et al. 2005)	*Pegaga*: 0.8 ± 0.1 (mg GAE/g) *Ulam raja*: 14.8 ± 0.3 (mg GAE/g) *Selom*: 3.4 ± 0.2 (mg/GAE/g) *Pucuk gajus*: 52.1 ± 1.0 (mg/GAE/g) *Daun kari*: 8.4 ± 0.3 (mg/GAE/g) *Cekur*: 2.5 ± 0.3 (mg/GAE/g) *Mengkudu*: 1.0 ± 0.0 (mg/GAE/g) *Selasih*: 6.4 ± 0.2 (mg/GAE/g) *Pudina*: 1.7 ± 0.1 (mg/GAE/g)
				Total phenolic content	Folin-Ciocalteau method	*Pegaga*: 0.3 ± 0.1 (mg GAE/g) *Ulam raja*: 0.3 ± 0.1 (mg GAE/g) *Selom*: 1.4 ± 0.1 (mg GAE/g) *Pucuk gajus*: 10.2 ± 2.6 (mg/GAE/g) *Daun kari*: 11.2 ± 0.3 (mg/GAE/g) *Cekur*: 3.7 ± 0.2 (mg/GAE/g) *Mengkudu*: 2.3 ± 0.1 (mg/GAE/g) *Selasih*: 25.5 ± 3.0 (mg/GAE/g) *Pudina*: 14.3 ± 1.2 (mg/GAE/g)
				DPPH free radical scavenging activity	(Brand-Williams et al. 1995)	*Pegaga*: 0.2 ± 0.0 (mg GAE/g) *Ulam raja*: 0.9 ± 0.2 (mg GAE/g) *Selom*: 2.5 ± 0.3 (mg/GAE/g) *Pucuk gajus*: 27.1 ± 0.8 (mg/GAE/g) *Daun kari*: 9.8 ± 1.1 (mg/GAE/g) *Cekur*: 1.5 ± 0.1 (mg/GAE/g) *Mengkudu*: 2.6 ± 0.3 (mg/GAE/g) *Selasih*: 1.0 ± 0.2 (mg/GAE/g) *Pudina*: 0.3 ± 0.1 (mg/GAE/g)

Continues TABLE 2.

Author	Title	Location	Extraction	Total polyphenol content / Antioxidant activity	Method	Results (unit)
				Ferric reducing antioxidant potential Total phenolic content	(Firuzi et al. 2005)	*Pegaga*: 0.7 ± 0.0 (mg GAE/g) *Ulam raja*: 11.0 ± 3.6 (mg GAE/g) *Selom*: 0.8 ± 0.1 (mg/GAE/g) *Pucuk gajus*: 27.6 ± 0.5 (mg/GAE/g) *Daun kari*: 7.4 ± 0.4 (mg/GAE/g) *Cekur*: 0.6 ± 0.1 (mg/GAE/g) *Mengkudu*: 1.3 ± 0.0 (mg/GAE/g) *Selasih*: 3.2 ± 0.2 (mg/GAE/g) *Pudina*: 4.7 ± 0.4 (mg/GAE/g)
(Chan et al. 2014)	Antioxidant properties of selected fresh and processed herbs and vegetables (2013)	Selangor, Malaysia	1 g of powdered sample extracted with 50 mL of methanol	Total phenolic content	Folin-Ciocalteau method	*Pucuk gajus*: 3890 ± 336 (mg GAE/100 g) *Kesum*: 2330 ± 283 (mg GAE/100 g) *Ulam raja*: 1880 ± 84 (mg GAE/100 g) *Selom*: 621 ± 63 (mg GAE/100 g) *Pegaga*: 247 ± 30 (mg GAE/100 g)
				Ferric reducing antioxidant potential	Using potassium ferricyanide assay	*Pucuk gajus*: 3260 ± 235 (mg GAE/100 g) *Kesum*: 2230 ± 149 (mg GAE/100 g) *Ulam raja*: 1110 ± 50 (mg GAE/100 g) *Selom*: 192 ± 12 (mg GAE/100 g) *Pegaga*: 147 ± 22 (mg GAE.100 g)
(Mohd Shukri et al. 2011)	Polyphenols and antioxidant activities of selected traditional vegetables (2011)	Seberang Perai Malaysia	5 g of powdered sample extracted in 10 mL methanol	Total phenolic content	Folin-Ciocalteau method	*Pucuk gajus*: 361 ± 18 (mg GAE/kg) *Pegaga*: 100 ± 7.8 (mg GAE/kg)
(Nooraini et al. 2015)	Total phenolic content and antioxidant activity of pure and formulated extracts of *kesum (Polygonum minus), bawang putih (Allivium sativum), pegaga (Centella asiatica)*, and *ulam raja (Cosmos caudatus)*	Johor, Malaysia	5 g of pure sample extract	Total phenolic content	Folin-Ciocalteau method (Mavundza et al. 2010)	*Kesum*: 1388.2 ± 111 (mg GAE/100 g) *Pegaga*: 150.01 ± 37.89 (mg GAE/100 g) *Ulam raja*: 323.59 ± 7.19 (mg GAE/100 g)
				DPPH free radical scavenging activity		*Kesum*: 84.45 ± 7.33 % *Pegaga*: 40.83 ± 26.95 % *Ulam raja*: 60.71 ± 6.74 %

Continues TABLE 2.

Author	Title	Location	Extraction	Total polyphenol content / Antioxidant activity	Method	Results (unit)
(Kongkachuichai et al. 2015)	Nutrients value and antioxidant content of indigenous vegetables from Southern Thailand	Chumphon, Surat Thani, Ranong, Nakhon Si Thummarat, Phatthalung, Trang, Satun, Krabi, Phang Nga, Phuket, Songkhla, Pattani, Yala and Narathiwat	2 g of homogenised samples were extracted by shaking at room temperature with 20 mL of 50% dimethyformamide	Total polyphenol content	Folin-Ciocalteau method	*Selom:* 239.23 ± 6.10 (mg GAE/100 g) *Pucuk gajus*: 4075.79 ± 54.24 (mg GAE/100 g)
				Ferric reducing antioxidant potential	(Benzie & Strain 1996)	*Pucuk gajus*: 36397.64 lmol TE/100 g)
(Andarwulan et al. 2010)	Flavonoid content and antioxidant activity of vegetables from Indonesia	Bogor, Indonesia	Pure extract	Total polyphenol content	Folin-Ciocalteau method	*Ulam raja*: 1.52 ± 0.11 (mg/g dw) *Pegaga*: 0.463 ± 0.018 (mg/g dw) *Beluntas*: 0.831 ± 0.129 (mg/g dw)
				DPPH free radical scavenging activity	(Brand-Williams et al. 1995)	*Ulam raja*: 112 ± 3 µmol TE/g dw *Pegaga*: 13.8 ± 0.39 µmol TE/g dw *Beluntas*: 96.4 ± 15.2 µmol TE/g dw
				Ferric reducing antioxidant potential	(Oyaizu 1986)	*Ulam raja*: 172 ± 1 µmol TE/g dw *Pegaga*: 38.3 ± 0.5 µmol TE/g dw *Beluntas*: 81.1 ± 0.6 µmol TE/g dw

et al. 1998). Sulaiman et al. (2011) reported that *kesum* has the highest DPPH radical scavenging activity followed by *pegaga* and *ulam raja*. The correlation between total phenolic content and antioxidant activity was rather weak (r=0.293) as phenolic compounds were not the only contributor to antioxidant activities. Furthermore, the type, quantity of phenolic compounds and the non-phenolic antioxidants may also affect the antioxidant activity of the plant extracts.

Mediani et al. (2014) has explained the central importance of drying methods in preserving the phytochemical compounds of *ulam raja*. The drying step prior to storage is necessary to maintain the quality of the herbs. The results indicated the variation of the TPC and antioxidant activity in the samples prepared by air drying, freeze drying and oven drying. In this study, air drying had the minimum influence on the phytochemical compounds, thus, can be applied for the sample preparation due to the acceptable levels of TPC and antioxidant activity and its low cost. Air drying method resulted in the highest free radical scavenging activity against 1,1-diphenyl-2-picrylhydrazyl (DPPH) (IC50 = 0.0223 mg/mL) and TPC (27.4 g GAE/100 g).

The effects of various food processing methods on the antioxidant properties of selected herbs and vegetables were analyzed and evaluated in one of Malaysian study (Chan et al. 2014). It was based on the DPPH radical scavenging activity. Processing methods applied on the tested *ulam* samples were blanching, microwaving, freezing, brining, and pickling. Among 10 fresh *ulam* assessed, the *pucuk gajus* showed the strongest antioxidant properties followed by *kesum* and *ulam raja*, *selom* and *pegaga*. Generally, *kesum, pucuk gajus* and *ulam raja* exhibited high DPPH radical scavenging activity among all selected *ulam*.

Ferric ion reducing activity of selected ulam Ferric reducing antioxidant power (FRAP) assay is usually carried out using the method described by Benzie and Strain (1996) as a measure of antioxidant power of *ulam* extracts. When ferric chloride reacts with 2,4,6-tripyridyl-s-triazine (TPTZ) at low pH level, ferric will be converted into ferrous causing formation of ferrous tripyridyl triazine complex. FRAP values are obtained by comparing the absorbance change at 593 nm in reaction mixture with those containing ferrous ions in known concentration. An antioxidant can prevent the generation of reactive oxygen species by metal chelation or enzyme-catalyzed removal of a potential oxidant in a redox reaction (Benzie & Strain 1999). In Reihani and Azhar (2012) study, it was reported that selom exhibited the highest ferric ion reducing activity followed by *ulam raja, daun kari, pegaga* and *petai*.

In Chan et al. (2014) study, *pucuk gajus* exhibited the strongest ferric reducing antioxidant potential followed by *kesum, ulam raja, selom* and *pegaga*. The ranking results were similar to the TPC. The highest correlation between total phenolic content and FRAP could be obtained from 70% methanol extracts. This 70% methanol is the most appropriate solvent for extracting phenolic compounds with FRAP property of *ulam* (Thaipong et al. 2006) study. In Sulaiman et al. (2011) study, the ferric ion reducing potential of 70% methanol extracts can be ranked in the following order: *pucuk gajus, ulam raja, daun kari, daun selasih, selom, cekur, daun pudina, mengkudu* and *pegaga*. In general, *pucuk gajus* exhibited the highest ferric ion reducing potential among all the selected *ulam*.

Role of polyphenols in improving cognitive decline The role of polyphenols in improving cognitive decline is shown in Figure 2. Cognitive decline is one of the alarming health issues which may cause dementia, illness and death. The cognitive decline may initiate from middle-aged onwards or even earlier (Deary et al. 2009). Aging is the strongest factor that causes cognitive decline. The most common brain changes that occur during aging is decreasing in white matter density and number of white matter lesions (Bartzokis 2003; Guttmann et al. 1998). Abnormalities of white matter are associated with reduced performance in processing speed, executive functions and immediate and delayed memory (Gunning-Dixon & Raz 2000). Oxidative stress is essentially an imbalance between the production of free radicals and the ability of the body to counteract or detoxify their harmful effects through neutralization by antioxidants and polyphenols (McCord 2000). A free radical is an oxygen containing molecule that has one or more unpaired electrons, making it highly reactive with other molecules. Oxygen by-products are relatively unreactive but some of these can undergo metabolism within the biological system to give rise to these highly reactive oxidants called reactive oxygen species (Gilgun-Sherki et al. 2001). However, free radicals can chemically interact with cell components such as DNA, protein or lipid and steal their electrons in order to become stabilized (Pham-Huy et al. 2008). Thus, it will eventually cause DNA damage, protein damage and lipid peroxidation. DNA damage will induce Cytochrome C release from damaged mitochondria, which will bind to apoptosis-activating factor-1 (Apaf-1) and causing activation of caspases and eventually apoptosis occurs (Schimmer et al. 2004). Prolong DNA damage can cause cognitive impairment among mild cognitive impairment (MCI) and Alzheimer's disease (AD) patient by oxidation of purines and pyrimidine in peripheral neurons. The single and double strands of primary DNA will be broken at the purine and pyrimidine structures as reported among MCI and AD patients compared to the healthy elderly population (Cooke 2006).

Oxidative stress may be one of factors of neurodegeneration in AD brains (Mao & Reddy 2011). Generation of oxidative stress is normally due to imbalance between reactive oxygen species (ROS) - producing pathways and (ROS)-scavenging pathways. Normally, the ROS production is due to mitochondria dysfunction (Navarro & Boveris 2008). Mitochondrion is one of the important organelle in aging and some comorbidities including cancer, diabetes, cardiovascular and neurodegenerative diseases (Martin 2010; Reddy 2008).

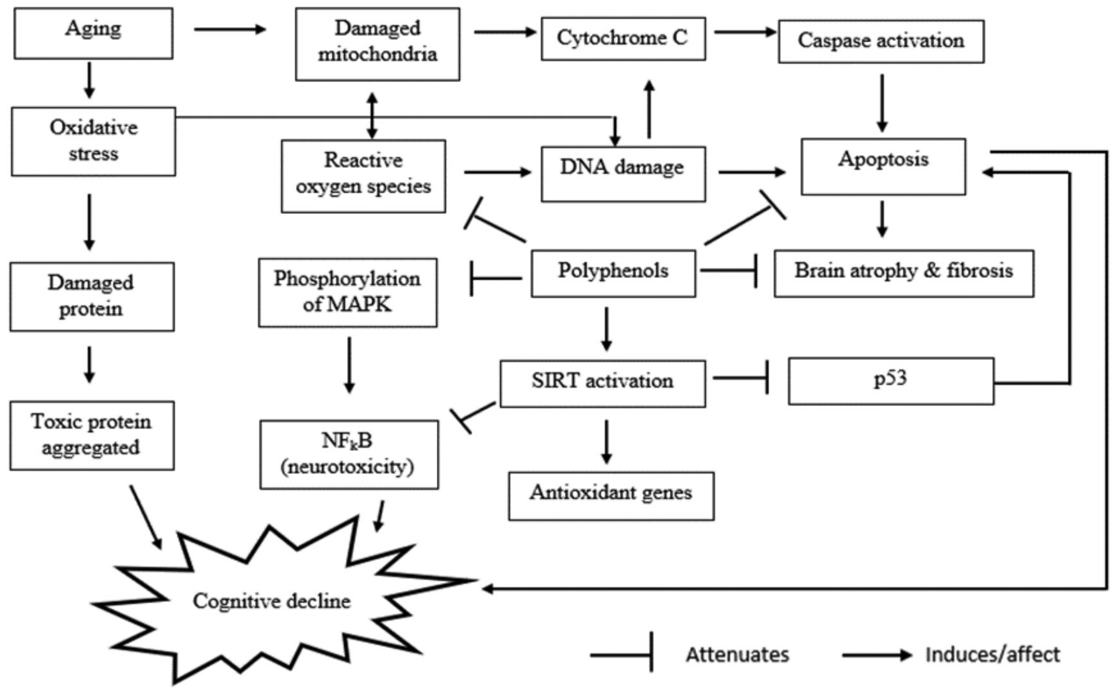

FIGURE 2. Brief diagram on the process leading to cognitive decline associated with polyphenols

Mitochondria dysfunction will cause reactive oxygen species (ROS) production, abnormal intracellular calcium levels and reduced in mitochondrial ATP (Hengartner 2000). Mutation of mitochondria DNA (mtDNA) structure can be seen among AD patients which is caused by misreading of oxidized bases during DNA replication process and it leads to nucleotide substitution. Eventually it will cause neuropathological changes in AD patients' brain and lead to severe neurodegenerative disease condition. If the number of mtDNA increases, it will cause mitochondria dysfunction and eventually lead to high ROS production. The increased generation of ROS can cause lipid peroxidation, protein damage, and several types of DNA lesions in cells (Lagouge & Larsson 2013). Mitochondria dysfunction will cause protein releases from the mitochondria that activate the caspase pathway leading to apoptosis, cell death and aging (Lagouge & Larsson 2013). Thus, this will then lead to Alzheimer's disease and other neurodegenerative diseases.

Inadequate polyphenols and antioxidants intake, iron overload, insulin resistance and aging are factors causing mitochondria dysfunction and oxidative stress among elderly population (Roussel & Ferry 2002). Aging process is a progressive condition that will cause the accumulation of oxidative damage to biomolecules such as nucleic acids, lipids, proteins and carbohydrates due to imbalance between pro-oxidants and antioxidants. Individuals with mild cognitive impairment may show high oxidative damage in the brain before the onset of dementia (Hedden & Gabrieli 2004).

On the other hand, polyphenols can cause sirtuins activation. Sirtuins is a type of protein which is encoded by a gene. They act as cell regulators in human body and play an important role in attenuating neurodegenerative diseases. Sirtuins is also called NAD-dependent deacetylase sirtuin-1 which is an enzyme that deacetylates proteins that contribute to cellular regulation in humans (Sinclair & Guarente 2006). Sirtuins specifically SIRT 1 can inhibit NF-kB-regulated gene expression which is a protein complex strongly linked to aging, degenerative disorders and even cancer. SIRT1 is responsible in deacetylation of p53 which will reduce the tendency of apoptosis of cells when exposed to damage (Sinclair & Guarente 2006). Furthermore, Nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB)-regulated gene expression is inhibited by deacetylating the RelA/p65 subunit of NF-κB at lysine 310 and SIRT1 activation (Kauppinen et al. 2013; Yeung et al. 2004). NF-κB is a protein which controls transcription of DNA and many genes involved in inflammation and high NF-κB also could cause schizophrenia due to inflammation and degeneration of neurons (Monaco et al. 2004; Song et al. 2009).

Polyphenol has the potential to inhibit mitogen-activated protein kinase (MAPK) signaling pathway by regulating the expression of inflammatory proteins and cytokines production which induced by lipopolysaccharide (LPS) and the activation of MAPK was reduced (Spagnuolo et al. 2017). MAPK is a type of protein kinase which regulate proliferation, gene expression, differentiation, cell survival and apoptosis (Pearson et al. 2001). The flavonoid could scavenge free radicals and reduce neuron apoptosis so that neuroinflammation is inhibited. One of the study reported that at the doses of 50-200 mg/kg of flavonoid-rich extract from *Rosa laevigata Michx* could reduce the pro-inflammatory markers (NF-κB, iNOS, COX-

2, MMP-9, TNF-α, IL-4, IL-6, IL-1β) expression followed by the reduction of the levels of p-JNK, p-ERK and p38 which involved in MAPK pathway (Zhang et al. 2013). In addition, quercetin, a bioactive compound was able to decrease inducible nitric oxide synthase (iNOS) expression which is involved in the stimulation of nitric oxide (NO) in microglial cells that trigger neurodegenerative disease (Bournival et al. 2012).

Neuroprotective effect of selected ulam Out of eight studies that had been reviewed in Table 3, only two studies were human trials carried out in Malaysia, a study was a systematic review in Thailand and the remaining studies were animal studies (*n*=5) in Malaysia and Indonesia. In addition, the randomized controlled trial studies involving *ulam* tablet supplementation to healthy adults and middle-aged women and assessed their cognitive function. Poor mental health will affect individuals as their age increases and cause the cognitive function decline.

Study by Udani (2013) reported a significant improvement in executive functioning, cognitive flexibility, reaction time and working memory after the intervention by providing 20 healthy subjects in Malaysia with *Superulam* capsules for 3 weeks. *Superulam* capsule is made up of combination extracts *sireh*, turmeric, *pegaga*, *daun kari*, *selasih*, *kesum* and *ulam raja*. When comparing capsule to placebo, the data showed a significant decrease in mood, angerand tension among capsule supplemented subjects (Udani 2013). The study by Shahar et al. (2015) reported that supplementation of two *Polygonum minus (kesum)* capsules (250 mg) taken once daily has the potential to improve mood and quality of life after 6 weeks of intervention compared to baseline among 35 to 55 years old middle-aged women (Shahar et al. 2015; Yahya et al. 2017). This result was supported by George et al. (2014) study which reported that *Polygonum minus* possesses antioxidant and anticholinesterase activity and demonstrated enhanced cognition *in vivo*. Cellular antioxidant protection from free radical damage was also observed in mice. *Polygonum minus* contains two bioactive compounds namely quercetin and quercetin-3-glucuronide which act as anti-depression agent. In one of *in vivo* studies, it was shown that quercetin could reduce stress-induced brain corticotropin-releasing factor (CRF) expression which would cause anxiety and depression.

Based on the conclusion made by a systematic review in Thailand, due to different doses and standardization of *Centella asiatica (pegaga)* used in the interventions, no strong evidence can be used to prove that *pegaga* can improve cognitive function. However, most of the studies reported that *pegaga* capsule supplementation could improve working memory, alertness and relieve anger. This result was obtained from a systemic review article which reviewed 11 articles related to relationship between *pegaga* consumption, particularly capsule supplementation with cognitive function and mood (Puttarak et al. 2017). *Pegaga* had been consumed to control anxiety as it helps in relaxation and mental calmness by inhibiting phospholipase substrate 2 activities in rat's cerebellum (Wijeweera et al. 2006). There are many *in vivo* studies which studied the central nervous system effects of *pegaga* but the clinical trials and human studies are still limited (Puttarak et al. 2017; Yogeswaran et al. 2016).

In addition to *Polygonum minus* and *Centella asiatica, Oenanthe javanica* leaves or *selom* has also been studied for its neuroprotective effect. One of the animal study indicated that *Oenanthe javanica* extract could improve cell proliferation and neuroblast differentiation by increasing brain-derived neurotrophic factor immunoreactivity in the rat dentate gyrus (Chen et al. 2015). *Oenanthe javanica* leaves or *selom* can be used for the development of products for memory improvement because it could inhibit acetylcholinesterase (AChE) activity and increase latency time in passive avoidance test (Won et al. 2015). In general, further human study on the supplementation of *Oenanthe javanica* is warranted to study the relationship with human cognitive function. Another 2 animal studies also reported that *Murraya koenigii* leaves increased acetylcholine level in brain and would improve memory of both young and aged mice (Tembhurne & Sakarkar 2010). Furthermore, it also could inhibit brain acetylcholinesterase enzyme and elevate the acetylcholine concentration in brain homogenate and also improving memory to prevent Alzheimer's disease (Mani et al. 2012). *Ocimum basilicum* leaves also reported to have neuroprotective property as it can reduce cerebral infarct size and lipid peroxidation, restoration of glutathione content and prevent Alzheimer's disease in mice (Bora et al. 2011).

FUTURE DIRECTIONS AND RESEARCH GAPS

Mild-cognitive impairment (MCI) is known to be intermediate stage between aging and dementia. Those populations with MCI have a high risk of developing dementia (Burns & Zaudig 2002). Individuals with dementia and Alzheimer's disease in the world are estimated to be doubled for every 20 years and reached 81 million by 2040 (Reitz et al. 2011). There are limited pharmacological treatment for Alzheimer's-related memory loss and dementia, thus it is important to assess the cognitive impairment at an early stage and exploring treatment and prevention measures are very crucial. In this review, *ulam* had been shown to be rich in polyphenols and antioxidants (Amalia et al. 2012; Bachok et al. 2014). To date, most studies were animal studies (*n*=5) and the limited human-based studies (*n*=3) resulted in inadequate evidence-based conclusions in the effects neuroprotective effects of *ulam* (Yogeswaran et al. 2016). Majority of studies used *ulam* tablet supplementation which needs higher financial resources, however less effective for long term measure. On the other hand, the consumption of *ulam* in raw form which is cheaper and more effective for long term measure (Nyaw & Nyaw 2010). In addition, although many studies conducted in the South East Asia have determined the TPC and antioxidant activities of *ulam,* the study on the relationship between the TPC and

TABLE 3. Previous studies on cognitive function in association with selected *ulam*

Author	Study design	Method	Participants	Outcomes
(George et al. 2014)	Experimental study	1. Determination of antioxidant capacity using ORAC assay 2. Determination of CAP-e antioxidant capacity 3. Determination of anticholinesterase activity 4. Barnes assay	2-6 months old adult male C57BL/6 mice (20-25 g), (n = 12-14)	This data shows that *P. minus* extract possesses antioxidant and anticholinesterase activity and demonstrated enhanced cognition *in vivo*. Cellular antioxidant protection from free radical damage was observed
(Shahar et al. 2015)	Randomized, double-blind, placebo-controlled study	1. Digit span 2. Comprehensive trail making test (CTMT) 3. Three domains of CNS vital sign (CNSVS) 4. Mood 5. Anthropometric measurements	35 Middle-aged women (35-55 years old)	Two capsules of *P. minus* supplementation (250 mg) was taken once daily has the potential to improve mood and quality of life after 6 weeks of intervention compared to baseline
(Udani 2013)	Randomized, double-blind, placebo-controlled crossover study	1. Computer-based testing of reaction time 2. Complex attention 3. Working memory 4. Sustained attention 5. Executive functioning 6. Profile of mood states 7. Chalder fatigue scale	20 healthy adults (35-65 years old)	There is a significant improvement in executive functioning, cognitive flexibility, reaction time and working memory after the intervention of consuming *Superulam* capsules. When comparing products to placebo, the data showed a significant decrease in mood, anger and tension
(Puttarak et al. 2017)	Systemic review and meta-analysis	1. Reviewed 11 articles related to *Centella asiatica* and cognitive function and mood	11 articles	Due to different doses and standardization of *Centella asiatica* intervention, there is not strong evidence to prove that *Centella asiatica* can improve cognitive function but most of the studies reported that it could improve working memory, alertness and relieve anger
(Mani et al. 2012)	Experimental study	1. Acute toxicity studies 2. Drug treatment 3. Elevated plus-maze 4. Passive avoidance paradigm 5. Collection of brain samples 6. Estimation of brain cholinesterase 7. BACE1 inhibitory activity	Male, Swiss Albino mice (Young (3-4 months) and aged (12-15 months) mice)	The total alkaloids extract of *Murraya koenigii* leaves increased acetylcholine level in brain and would improve memory of both young and aged mice. This study indicates it is useful in managing Alzheimer's disease and dementia

Continues TABLE 3.

Author	Study design	Method	Participants	Outcomes
(Tembhurne & Sakarkar 2010)	Experimental study	1. Acquisition and retrieval memory in elevated plus 2. maze (EPM) 3. Sodium nitrite intoxication 4. Biochemical Estimations for brain cholinesterase 5. and serum cholesterol 6. Estimation of brain cholinesterase	Male Swiss Albino Mice (Aged (12-15 month's)	The ethanolic extract of *Murraya koenigii* leaves has lowering effect in serum cholesterol in aged mice and also inhibiting brain acetylcholinesterase enzyme. It elevated the acetylcholine concentration in brain homogenate and also improving memory to prevent Alzheimer's disease
(Bora et al. 2011)	Experimental study	1. Assessment of cerebral infarct size 2. Estimation of thiobarbituric acid reactive substance (TBARS) 3. Evaluation of short-term memory using elevated plus maze 4. Inclined beam walking test 5. Lateral push test	Swiss albino mice of either sex	*Ocimum basilicum* leaves have neuroprotective property as it can reduce cerebral infarct size and lipid peroxidation, restoration of glutathione content and attenuation of motor dysfunctions. It is safe and suggested to use clinically in stroke prevention
(Chen et al. 2015)	Experimental study	1. Tissue processing for histology Immunohistochemistry	14 male Wistar rats (aged 5 Weeks)	These results indicate that *Oenanthe javanica* extract improves cell proliferation and neuroblast differentiation by increasing brain-derived neurotrophic factor immunoreactivity in the rat dentate gyrus

antioxidant activity of *ulam* with cognitive status is still lacking. Therefore, it is crucial to conduct human studies to determine the effectiveness of polyphenol rich *ulam* that can contribute to reduction of cognitive decline. Biofluid samples including urine, blood and faeces may be collected and analyzed using metabolic profiling methods to discover the novel biomarkers of *ulam* intake and cognitive function-associated metabolites. The results of this study will identify the high potential *ulam* to be incorporated in the daily diet in order to prevent or manage symptoms and problems related to poor mental health and cognitive function. There is a potential for *ulam* to be commercialised as fortified food products in order to increase its outreach in global market.

CONCLUSION

In this review, traditional vegetables or *ulam* was found to be rich in polyphenols, antioxidants and contains medicinal properties such as neuroprotective effect. *Centella asiatica (pegaga), Oenanthe javanica (selom)*, *Polygonum minus (kesum), Ocimum basilicum (daun selasih)* and *Murraya koenigii (daun kari)* have the potential to improve cognitive function and mood improvement but more clinical studies should be undertaken to confirm the role of these *ulam* and others as neuroprotective agent.

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