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Korean traditional foods as antiviral and respiratory disease prevention and treatments: A detailed review

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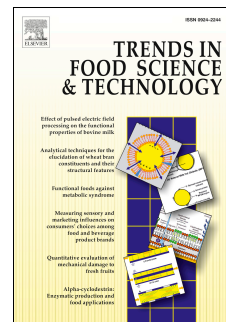
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1 **Korean traditional foods as antiviral and respiratory disease**  
2 **prevention and treatments: a detailed review**

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27 **Abstract**

28 *Background:* Korean traditional food (KTF), originated from ancestral agriculture and  
29 the nomadic traditions of the Korean peninsula and southern Manchuria, is based on  
30 healthy food that balances disease prevention and treatment. Fermented foods that  
31 include grains, herbs, fruits, and mushrooms are also an important practice in KTF,  
32 providing high levels of *Lactobacilli*, which confer relevant health benefits, including  
33 antiviral properties. Some of these probiotics may also protect against the Influenza  
34 virus through the modulation of innate immunity.

35 *Scope and Approach:* The emerging of the COVID-19 pandemic, in addition to other  
36 diseases of viral origin, and the problems associated with other respiratory disorders,  
37 highlight how essential is a healthy eating pattern to strengthen our immune system.

38 *Key Findings and Conclusions:* The present review covers the information available on  
39 edible plants, herbs, mushrooms, and preparations used in KTF to outline their multiple  
40 medicinal effects (e.g., antidiabetic, chemopreventive, antioxidative, anti-inflammatory,  
41 antibacterial), emphasizing their role and effects on the immune system with an  
42 emphasis on modulating properties of the gut microbiota that further support strong  
43 respiratory immunity. Potential functional foods commonly used in Korean cuisine  
44 such as Kimchi (a mixture of fermented vegetables), Meju, Doenjang, Jeotgal, and  
45 Mekgeolli and fermented sauces, among others, are highlighted for their great potential  
46 to improve gut-lung immunity. The traditional Korean diet and dietary mechanisms that  
47 may target viruses ACE-2 receptors or affect any step of a virus infection pathway that  
48 can determine a patient's prognosis are also highlighted. The regular oral intake of  
49 bioactive ingredients used in Korean foods can offer protection for some viral diseases,

50 through protective and immunomodulatory effects, as evidenced in pre-clinical and  
51 clinical studies.

52 **Keywords:** antiviral, pathogens, coronavirus, COVID-19, SARS-CoV-2, functional  
53 foods, plant extracts, respiratory infections, viruses, Korean traditional diet

54

## 55 **1. Introduction**

56 The positive health effects of several beverages and foodstuffs have been  
57 recorded and studied during the last decades. These effects are due to the presence of  
58 specific naturally-occurring compounds, whose particular levels and proportions  
59 influence the observed health benefits (Visioli, et al., 2011). In this context, several  
60 traditional Korean foodstuffs are currently recognized for their beneficial properties (Im  
61 Kim, Sim, & Choi, 2010). This fact is rationalized since, for Koreans, the low risk of  
62 diseases and feeding starts from the same root, based on the philosophy called  
63 “*Yaksikdongwon*,” which defends that good health is part of an appropriate diet, in  
64 order to keep the human body in balance (Oktay & Ekinici, 2019). According to this  
65 philosophy, medicinal therapy would only be required if a positive evolution of the  
66 disease is not observed after ‘treatment’ with food, since health starts with diet (Oh,  
67 Park, Daily III, & Lee, 2014). Therefore, in the same concept, medicine and food  
68 converge (Leem & Park, 2007). In other words, Korean traditional food (KTF) is based  
69 on a notion of healthy foods, and these healthy properties cover food materials and their  
70 preparation (H. Park & Kim, 2014; K. Y. Park, Jeong, Lee, & Daily, 2014). Such  
71 features have specialized over centuries owing to geographical, social, and political  
72 factors (Oh, et al., 2014).

73           Originating in ancient agriculture and nomadic traditions of the Korean  
74 peninsula and southern Manchuria, KTF has evolved through complex interactions  
75 between the environment and different cultural trends, developing a distinct ethnicity  
76 and a matchless culture (e.g., language and food) (Hyun Kim, Song, & Potter, 2006). In  
77 order to resist long winters within a land isolated by rugged mountains and rocky ocean  
78 fronts, KTF developed out of the obligation to preserve good food by fermentation  
79 (e.g., fish, seaweed, vegetables, and salted beans, among others) in clay pots  
80 (Dharaneedharan & Heo, 2016; Jayanta Kumar Patra, Das, Paramithiotis, & Shin,  
81 2016).

82           Apart from the fact that Koreans have learned a reasonable balance between  
83 nutrition and disease prevention/treatment, an increasing interest in South Korea  
84 opened up a market that includes dietary supplements and health products of natural  
85 origin (namely, functional health foods (FHF)) (Ji Yeon Kim, Kim, & Lee, 2008; Yoon,  
86 et al., 2012). Thus, a regulatory venue for such products in South Korea (one of the  
87 largest Asian markets for FHF) was introduced and regulated by the Korea Food and  
88 Drug Administration (KFDA) (Zawistowski, 2008).

89           Some herbs and fruits (such as ginseng, cinnamon, wormwood, ginger,  
90 pomegranate, and adlay) are actually used as food, but their therapeutic effects are also  
91 exploited. Therefore, KTF usually includes some herbs/fruits for their medicinal  
92 properties and, correspondingly, health benefits in KTF are attributed to various  
93 common ingredients (Hyun Kim, et al., 2006; H. Park & Kim, 2014). Based on this  
94 fact, KTFs are a subject of growing interest worldwide (Baeg & So, 2013; E. Y. Kim,  
95 2013). Particular KTF ingredients (broadly consumed in Korea) are currently being  
96 placed on global FHF markets, owing to the increasing interest beyond the

97 characteristic examples (e.g., ginseng preparations, mushrooms, fermented sauces and  
98 mixed rice). Such attention comes from increasing research supporting their several  
99 health benefits (H. Park & Kim, 2014), including antiviral properties (K.-D. Kang, et  
100 al., 2011; M. H. Lee, Lee, Lee, & Choi, 2013).

101 Antivirals are the only drugs traditionally used to treat infectious diseases of  
102 viral origin (Gonçalves, et al., 2020). However, like other drugs, they also have  
103 associated risks or harmful health effects, such as phlebitis, hematuria, hypocalcemia,  
104 creatininemia, and, in the worst cases, mutagenesis, and teratogenesis. Additionally,  
105 they develop resistance due to the change and decreased affinity of viral enzymes,  
106 especially polymerases and reverse transcriptases (Goldhill, et al., 2018; Gonçalves, et  
107 al., 2020). Therefore, the antiviral capacity of phytochemicals present in extracts of  
108 certain medicinal and edible plants and mushrooms (in common/dietary use) is a good  
109 choice, since they have been shown to be active *in vitro* and *in vivo* against many  
110 different types of viruses, including those that cause respiratory diseases (Nugraha,  
111 Ridwansyah, Ghozali, Khairani, & Atik, 2020; Verma, et al., 2020).

112 In this regard, acute respiratory infections present morbidity and mortality of  
113 approximately 4 million children annually. These infections are considered a major  
114 cause of early childhood mortality, including diarrhea and malnutrition (Rodríguez,  
115 Cervantes, & Ortiz, 2011). In fact, a shocking surprise in the scientific and global  
116 community was caused by the epidemiological situation initiated by the influenza A  
117 subtype H1N1. It is a swine-origin influenzavirus strain producing critical respiratory  
118 infection in some places, which was identified for the first time in April 2009  
119 (Phaswana-Mafuya, et al., 2020). However, the current situation (i.e., 2021) is even  
120 worse due to the pandemic generated by COVID-19, an emerging disease triggered by

121 SARS-COV-2 (severe acute respiratory syndrome coronavirus 2) (Rajaiah, Abhilasha,  
122 Shekar, Vogel, & Vishwanath, 2020). This disease has caused 3.03 million deaths  
123 worldwide as of this writing (i.e., 18/04/2021).

124 Therefore, without a cure or well-proven vaccine until now against SARS-  
125 COV-2 and the problems associated with other respiratory infections, a healthy eating  
126 pattern is essential to strengthen our body's defenses and improve response to these  
127 respiratory disease-causing agents (BourBour, et al., 2020; Lin, et al., 2016). Faced  
128 with the restrictions that we are currently experiencing, it is crucial to take care of our  
129 diet to maintain our health and ensure the strengthening of our immune system, that is,  
130 our body's natural defense against respiratory infections (Jawhara, 2020; Junaid, et al.,  
131 2020; Roy, et al., 2020). Therefore, it is easy comprehensible that a well-balanced diet  
132 is key to body homeostasis and in to preventing respiratory infections. Various  
133 nutrients in the diet on a regular basis can help strengthening the respiratory system.  
134 Moreover, more recently, studies have also highlighted the role of probiotics in  
135 promoting a healthy gut microbiota and how that can affect general health, reducing  
136 inflammation and strengthening the immune system. Adding to this, many people have  
137 to live with chronic conditions such as asthma, chronic obstructive pulmonary diseases  
138 (COPD) and pulmonary fibrosis that affect their quality of life. Lifestyle modification  
139 can help to protect the respiratory system and even reduce lung damage and disease's  
140 symptoms. Specific nutrients and foods have been identified to be particularly  
141 beneficial for lung function. Clinical studies have recommended that zinc, curcumin,  
142 and zinc-ionophores have significant antiviral potentials. And thus, intake of these food  
143 supplements can be helpful in the treatment of COVID-19 in the form of considerable  
144 immunity support, inhibition of replication of RNA of the SARS-COV-2 virus and by

145 prevention of the virus entry into the cell (Celik, Gencay, & Ocsoy, 2021; Ghati, et al.,  
146 2021; Roy, et al., 2020). Moreover, KTF offers good edible alternatives to help us in  
147 this purpose through prophylactic and direct actions (H. Park & Kim, 2014).  
148 Accordingly, the present narrative review covers the information available on edible  
149 plants, herbs, and preparations used in KTF to outline the potential of KFTs and their  
150 ingredients based on their antiviral and anti-respiratory effects.

151

## 152 **2. Korean traditional foods in brief and their beneficial effects**

153 Korean traditional foods (KTF) are known worldwide for being spicy, tasty, and  
154 delicious, but KTF are also able to promote wellbeing and a balanced health. This KTF  
155 characteristic is often linked with the obesity percentage of South Koreans (i.e., 3.5%),  
156 which differs substantially from other countries such as the United States, the United  
157 Kingdom, Brazil, Mexico or New Zealand (25-34%) (Gupta et al., 2012; Groneberg et  
158 al., 2015). This is a good starting point since such a low obesity rate can be attributed to  
159 the genetic factors of Asians compared to Caucasians since the latter are greater than  
160 the former, but this is also not entirely true. Nutritional habits of Koreans make them  
161 healthier than other people since the fat content of Korean food is generally 13% lower  
162 compared to American and European diets (Lee et al., 1999). This condition can be  
163 justified as Korean food culture has evolved from very ancient times and adheres to a  
164 significant classification of various philosophical actions. The recognition that  
165 consuming healthy food can prevent and cure diseases is deep-rooted Korean thinking  
166 (Oh et al., 2014).

167 In this sense, edible plants and mushrooms in KTF are exploited for their  
168 medicinal properties that support their health benefits. However, each KTF exhibits



169 particular benefits on health due to certain active principles and the use of special  
170 preparation/cooking procedures and practices (Patra et al., 2016). In addition, some  
171 KTF-used ingredients are also employed in traditional medicine to treat different health  
172 events. For instance, stomach problems are treated with chives or raw potato juice,  
173 whereas garlic is used for digestive purposes and blood cleansing. Bellflower roots and  
174 hazelnut are good for coughing/cold and skin/pregnant women, respectively, while  
175 patients are strengthened with pine nuts or rice porridge (Oktay and Ekinici, 2019).

176 The facts mentioned above supported several of the informed benefits of KTF  
177 and their ingredients (e.g., red ginseng, aloe, zedoary, turmeric, red sage, astragalus,  
178 among others), which comprise several effects, such as lower risks of cardiovascular  
179 diseases (Jovanovski et al., 2014), as well as neurological diseases (Leem and Park,  
180 2007), reduced probabilities of developing some cancer types due to anticancer  
181 properties (Yoon et al., 2013), more efficient and stronger internal organs (mainly liver  
182 and kidneys) (Choi, 2008), healthier digestion due to enhanced inclination for more  
183 digestible foods (Kim et al., 2006a), stronger bones by consuming isoflavones occurred  
184 in mushrooms/beans (Youn et al., 2008), and healthier skin (Pazyar et al., 2012).

185 A previous review categorized the impact of the ingredients of Korean edible  
186 herbs involving properties such as antidiabetic, chemopreventive, and antioxidative and  
187 effects on the immune system (Park and Kim, 2014). In the case of mushrooms (e.g.,  
188 *Agaricus blazei*, *A. bisporus*, *Flammulina Velutipes*, *Ganoderma lucidum*, *Hericiium*  
189 *erinaceus*, *Inonotus obliquus*, *Lentinus edodes*, *Phellinus linteus*, *Pleurotus eryngii*, *P.*  
190 *ostreatus*, *Sparassis crispa*, among several others), they were traditionally used in  
191 Korea for their health benefits (i.e., digestive effects, risk of cancer, lowering  
192 cholesterol, losing weight, improving the immune system, preventing diabetes and

193 anemia) (Thu et al., 2020), but also as food due to the good content of digestible  
194 carbohydrates and proteins and lower fat (Fu et al., 2002; Kim et al., 2008). Indeed, the  
195 antiviral effects of *I. obliquus* have been recognized, even against SARS-CoV-2  
196 (Shahzad et al., 2020).

197         Apart from using medicinal ingredients in KTFs within the healthy philosophy,  
198 the preparation is also important for them. In such preparations, preservation by  
199 fermentation is also an important practice in KTF, despite the country's different  
200 traditions (Han et al., 1993). As one of the cheapest methods to increase the shelf-life of  
201 several highly-perishable foods (e.g., vegetables, fruits, fish, and meat), fermentation is  
202 a microorganism-mediated transformation process of organic compounds (Lee et al.,  
203 2015). The importance of this process in KTF is the action of particular  
204 microorganisms (such as bacteria and yeasts), not only for transform organic  
205 compounds (particularly carbohydrates) but also for the role as probiotics, conferring  
206 important health benefits to feeders, and regular consumption is recommended (Park et  
207 al., 2014).

208         The most recognized Korean fermented probiotic food is *Kimchi* (a Korean  
209 mixture of Fermented Vegetables), which has more than 3,000 years of history (Chang,  
210 2018). It is widely consumed in South Korea and, together with Indian lentils, Spanish  
211 olive oil, Greek yogurt, Japanese soybeans, it is considered one of the five healthiest  
212 foods in the world (Dharaneedharan and Heo, 2016). In fact, a strain of  
213 *Lactiplantibacillus plantarum* isolated from *Kimchi* can modulate innate immunity and  
214 protect against IV (influenza virus) (Park et al., 2013) and produces cyclic dipeptides  
215 that inhibit IV proliferation (Kwak et al., 2013). However, other traditional Korean  
216 fermented foods can be highlighted, such as *Meju*, *Doenjang*, *Jeotgal*, and *Mekgeolli*,

217 which exhibit several medicinal effects (e.g., anticancer, antiobesity, antioxidant, anti-  
218 inflammatory, antidiabetes, among others) and involve different beneficial  
219 microorganisms, such as *Leuconostoc mesenteroides*, *L. plantarum*, *Aspergillus* sp.,  
220 *Bacillus* sp., *Bacillus siamensis*, *Halomonas* sp., *Kocuria* sp., *Saccharomyces*  
221 *cerevisiae*, among others (Dharaneedharan and Heo, 2016).

222

### 223 3. Korean Traditional Foods with Effects Against the Respiratory Diseases

224 Fermented foods have been widely studied, and their benefits for human health  
225 have been elucidated. In this sense, it has been shown that fermented foods can affect  
226 the modulation of the immune system; therefore, fermented foods may improve the  
227 immunitary response to certain diseases or infections, such as those caused by viruses.  
228 Fermented food by lactic acid bacteria has been described to produce metabolites with  
229 antiviral effects (Table 1). Some of the antiviral mechanisms of lactic acid bacteria are  
230 the stimulation of the immune system and the production of antiviral metabolites. This  
231 type of fermented foods has shown an antagonist effect on respiratory viruses, such as  
232 influenza virus by stimulating the immune response, such as increased levels of  
233 interferon (INF- $\alpha$  and INF- $\beta$ ) and interleukin (IL-6), as well as the high secretion of  
234 cytokines IL-2, IL-12, and IFN- $\gamma$  (Özel & Öztürk, 2020).

235 Kimchi is a well-known fermented traditional Korean food rich in vitamins,  
236 minerals and dietary fiber, containing lactic acid bacteria and other compounds.  
237 Kimchi's effects on health, extend to anti-obesity, anti-aging, anti-mutagenic, anti-  
238 cancer, antioxidant, and anti-diabetic roles (E.-K. Kim, Ha, Choi, & Ju, 2016; Y. S.  
239 Kwon, Park, Chang, & Ju, 2016; K. Y. Park, et al., 2014). Likewise, *Kimchi* contains  
240 lactic acid bacteria, which are related to the content of beneficial compounds to health,

241 as well as probiotic effects, decreased lipid peroxidation, and enhanced immune system  
242 response, reported *in vitro* and *in vivo* (Jang, Yu, Lee, & Paik, 2020; K. W. Lee, et al.,  
243 2016; S.-J. Yang, et al., 2019). Similarly, Rather, Choi, Bajpai, and Park (2015)  
244 demonstrated that a strain of *Lactiplantibacillus plantarum* (YML009) isolated from  
245 Kimchi has antiviral activity against the influenza virus H1N1 is hypothesized to be  
246 more effective than Tamiflu. Also, M.-K. Park, et al. (2013) found that  
247 *Lactiplantibacillus plantarum* DK119 (DK119) isolated from Kimchi improves  
248 protection for mice against the H1N1 influenza virus by intranasal and oral  
249 administration. Jang et al. have reported the immune-stimulating potential of the  
250 *Lactobacillus plantarum* Ln1 strains isolated from the Kimchi (Jang, et al., 2020).

251 On the other hand, Y. S. Kwon, et al. (2016) reported that kimchi intake might  
252 be associated with rhinitis prevention because Korean adults who consume *Kimchi* are  
253 less prone to asthma (H. Kim, et al., 2014). These effects may be related to vegetables  
254 and lactic acid composition of *Kimchi*, since the consumption of this food provides a  
255 significant amount of vitamins, such as ascorbic acid, which is associated with the  
256 improvement of the immune system and prevents allergic diseases such as rhinitis  
257 and asthma (E.-K. Kim, et al., 2016; H. Kim, et al., 2014). In this sense, H. Kang, et al.  
258 (2009) demonstrated that bacteria presented in Kimchi could be responsible for the  
259 reduction of allergic diseases (such as rhinitis and asthma) in a murine model, as they  
260 have found that *Leuconostoc citreum* HJ-P4 (KACC 91035) isolated from *Kimchi*  
261 improves the immune system by decreasing serum levels and enhancing the secretion  
262 of antigen-specific IFN- $\gamma$ . Likewise, Hee Kang, Moon, Lee, and Han (2016) have found  
263 that the bacterium *Leuconostoc citreum* EFEL2061, isolated from Kimchi, induced  
264 cytokines and decreased the serum IgE in an allergic mice model. They reported that

265 this could be due to the enhance in innate immune cells and reduced the bystander B  
266 cell activation. Also, Won, et al. (2011) reported that strains of *Lactobacillus* isolated  
267 from Korean fermented foods (*Kimchi* and *Deodoek Muchim*) have a positive effect on  
268 improving the immune system in the murine model; they found that this effect could be  
269 due to the increased secretion of IL-2 which could induce T-lymphocytes proliferation  
270 and IFN- $\gamma$  production; therefore these bacteria can affect diseases like asthma (Ya, et  
271 al., 2008).

272 On the other hand, fermented Korean food, such as "doenjang" has been studied  
273 for the prevention of asthma; in this sense, J. Song, et al. (2019) demonstrated that a  
274 bacterium isolated from the fermented Korean food "doenjang" has a protective effect  
275 against allergic asthma in a murine model. They found that the administration of  
276 *Staphylococcus succinus* strain 14BME20 significantly reduced cytokines and induced  
277 the accumulation of anti-inflammatory cells, enhancing the immune response to  
278 allergens. Likewise, Bae, Shin, See, Chai, and Shon (2014a) reported that an ethanol  
279 extract from the traditional Korean fermented soybean food, namely "*Cheonggukjang*"  
280 decreased the symptoms of allergic asthma in a murine model; they found that this  
281 extract decreased  $\text{Ca}^{2+}$  input to mast cells and decreased degranulation and histamine  
282 release from mast cells. Wei et al. (2015) also reported the antiviral effect of extracts of  
283 *chongkukjang* against the influenza A virus. They found that ethyl acetate extract from  
284 *chongkukjang* showed inhibitory activity of neuraminidase *in vitro*. Also,  
285 *chongkukjang* extracts maintained higher body weight and decreased the mortality of  
286 influenza in infected mice. Besides, E. K. Kim and Ju (2019) found that the  
287 consumption of seaweed and fish could be related to the prevention of asthma in  
288 Korean adults because these foods have a great content of polyunsaturated fatty acids

289 and vitamins, related to anti-inflammatory precursors and pro-inflammatory mediators,  
290 such as protectins, resolvins, prostaglandins, and leukotrienes.

291 Besides, the Korean Red Ginseng which is obtained by the processing of the  
292 ginseng using repeated steaming and drying has shown numerous potential activity  
293 against the human pathogenic viruses such as human immunodeficiency virus, human  
294 herpes virus, influenza virus, respiratory syncytial virus, hepatitis virus, norovirus,  
295 enterovirus, rhinovirus, coxsackievirus and rotavirus (Im, Kim, & Min, 2016). It is  
296 stated that the ginseng could possibly exert a direct antiviral potential by a number of  
297 mechanism of action such as inhibiting the attachment of the virus, penetration and  
298 replication and also through the enhancement of the host immunity (Im, et al., 2016). In  
299 another study it has been reported that the major compound in ginseng called the  
300 ginsenosides are highly effective against the H1N1, H3N2, H5N1 and H9N2 influenza  
301 viruses by the stimulation of the antiviral cytokines (Chan, et al., 2011; Dae-Goon Yoo,  
302 et al., 2012; E. H. Park, et al., 2014; Ratan, et al., 2020). A clinical study has also  
303 reported that the Korean red ginseng have reduced the depletion of CD4 T-cells and  
304 have weakened the serum soluble CD8 antigen level in patients infected with the HIV  
305 type-1 viruses (Y.-K. Cho & Kim, 2017; Ratan, et al., 2020). Another herb, *Geranii*  
306 *Herba* (*Geranium thunbergii* Siebold et Zuccarini), which is has been included in the  
307 Korean traditional foods, have been reported to possesses antiviral effects against the  
308 influenza viruses through the mechanism of neuraminidase enzyme inhibition (J.-G.  
309 Choi, Kim, Kim, & Chung, 2019). In another study, the authors have reported that  
310 Platycodin D, a natural bioactive compound found in *Platycodon grandiflorum*, are  
311 helpful in preventing both the lysosome- and TMPRSS2-driven COVID-19 infection by  
312 obstructing the membrane fusion mechanism and or by briefly disrupting the

313 distribution of membrane cholesterol (T. Y. Kim, et al., 2021). Similarly another herbal  
314 formulation, *Qingfei Paidu* decoction included in both Korean and Chinese  
315 Pharmacopea, are helpful in the treatment of COVID-19, as it could inhibit and  
316 alleviate the excessive immune responses and eliminate the inflammation by regulating  
317 the immune-related pathways and cytokine action-related pathways (Wu, et al., 2020;  
318 Zhao, Tian, Yang, Liu, & Zhang, 2020). This herbal formulation increases the  
319 immunity and reduces inflammation by targeting the lung and spleen in COVID-19  
320 patients (Wu, et al., 2020; Zhao, et al., 2020).

### 321 ***3.1 Korean traditional foods and beneficial effects on the COVID-19***

322 Korean meals are rich in grains and vegetables, and many publications have  
323 arisen describing their pharmacological properties. A number of traditional foods have  
324 been reported to possess beneficial antiviral effects against the the COVID-19 virus and  
325 these foods and herbs could be taken as dietary supplements and thus could be helpful  
326 in preventing the infection and strengthening the immunity against these viruses  
327 (Panyod, Ho, & Sheen, 2020). Besides, a number of research has been reported on the  
328 numerous medicinal plants and their potential active components which are highly  
329 effective against the COVID-19 viruses by possibly blocking the life-cycle related  
330 proteins such as the cellular receptor ACE2, papain-like or chymotrypsin-like  
331 proteinases or by other possible mode of actions (Ang, Lee, Kim, Choi, & Lee, 2021;  
332 Benarba & Pandiella, 2020). Cabbage and fermented vegetables, for instance, fall under  
333 the scope of anti-viral properties (and severe anti-COVID-19 symptoms) (Bousquet, et  
334 al., 2020). In the case of COVID-19 (SARS-CoV-2 infections), there is a correlation  
335 with lower mortality rates due to the high consumption of fermented vegetables,  
336 common in East Asia, Central Europe, and the Balkans.

337           These foods contain many *Lactobacilli*, which are also effective activators of  
338 nuclear factor (erythroid-derived 2)-like 2 (Nrf2). Additionally, *Lactobacilli*, present in  
339 large amounts in the fermented foods with strong probiotic properties are effective  
340 against the foodborne pathogenic microfloras (Behera, Ray, & Zdolec, 2018).  
341 Previously, heat-killed *Lactobacilli* have already been reported to effectively protect  
342 against influenza A and prevent secondary infections by stimulating immunity (Jung, et  
343 al., 2017). A number of recent publications already exist, establishing a relationship  
344 between diet, gut microbiota, and viral and respiratory infections (Alkhatib, 2020;  
345 Chaari, Bendriss, Zakaria, & McVeigh, 2020). This literature attempts to draw  
346 correlations and make practical recommendations for the use of antiviral functional  
347 foods and lifestyle approaches to tackle the ongoing COVID-19 pandemic. They based  
348 their reports on the latest knowledge on the immunology of COVID-19 (Vabret, et al.,  
349 2020) and the reported effects of the gut microbiome on health and disease.

350           However, before the pandemic of COVID-19 erupts, there were already  
351 comprehensive reports on the value of foods for their nutritional, antioxidant activity,  
352 and phenolic composition, including beans, which are widely used by Koreans (Carbas,  
353 et al., 2020). Moreover, many publications have also highlighted the role of microbiota  
354 on viral infections (Dominguez-Diaz, Garcia-Orozco, Riera-Leal, Padilla-Arellano, &  
355 Fafutis-Morris, 2019; Planès & Goujon, 2020; Roth, Grau, & Karst, 2019; Wilks &  
356 Golovkina, 2012). Indeed, much has been postulated about how the gut microbiome  
357 can influence the severity of COVID-19. The greatest risk is often associated with pre-  
358 existing conditions as hypertension, diabetes, and obesity (Richardson, et al., 2020), as  
359 already recognized by official health organizations such as the Centers for Disease  
360 Control and Prevention, CDC, U.S.A. ( [15](https://www.cdc.gov/coronavirus/2019-</a></p></div><div data-bbox=)



361 [ncov/need-extra-precautions/people-with-medical-conditions.html](https://www.cdc.gov/ncov/need-extra-precautions/people-with-medical-conditions.html) accessed Dec 29th,  
362 2020). A relationship between all of these conditions and alterations in the gut  
363 microbiome composition was reported (Aoun, Darwish, & Hamod, 2020; Gurung, et  
364 al., 2020; Jose & Raj, 2015). The robustness of these associations raise the possibility  
365 that the mechanisms underlying hypertension, diabetes, and obesity may be responsible  
366 for developing severe respiratory infections associated with COVID-19; the gut  
367 microbiome at the time of infection may be determinant for patients outcome.

368 COVID-19 disease is caused by the new beta-coronavirus, now designated  
369 SARS-CoV-2 (Severe Acute Respiratory Syndrome coronavirus 2). The global  
370 COVID-19 pandemic has started an unprecedented race to find therapeutic targets and  
371 treatments for this disease and related serious pulmonary infections; thus, everything  
372 about SARS-CoV-2 has been under tight scrutiny. SARS-CoV-2 shares 79% sequence  
373 identity with SARS-CoV. This virus provoked a previous outbreak in early 2000, and  
374 with MERS-CoV, the Middle East Respiratory Syndrome Coronavirus (~50%) that  
375 appeared in 2012 (Lake, 2020; R. Lu, et al., 2020). In common, all of these pathogens  
376 use the angiotensin-converting enzyme II (ACE-2) receptor to enter into the cell and  
377 have distinctive spike proteins. ACE-2 receptors are also expressed in cardiovascular  
378 tissues and kidneys, and gastrointestinal (GI) tracts, besides the airways (Harmer,  
379 Gilbert, Borman, & Clark, 2002; Leung, et al., 2020). Thus, the expression of receptors  
380 for this peptidase is decisive for COVID-19 patient outcomes and has been pinpointed  
381 as a high-potential target for an effective vaccine. Moreover, it has been reported that  
382 SARS-CoV2 RNA can be detected in the stool of some patients with COVID-19 long  
383 after the live virus can be cultured from patients' secretions and feces. Together with  
384 the fact that many patients develop diarrhea as a symptom of COVID-19, this suggests

385 a distinct gut-lung link that may encompass gut microbiota (Dhar & Mohanty, 2020;  
386 Zuo, et al., 2020).

387 The gut-lung or axis connection was reported long before the COVID-19  
388 outbreak (Anand & Mande, 2018). A recent review points to the role of gut-lung axis in  
389 modulating the immune response and its implication in respiratory pathologies (Enaud,  
390 et al., 2020). The gut microbiota may likely predict the patient's prognosis for SARS-  
391 CoV-2 infection, particularly when considering reports of gut symptoms (such as  
392 diarrhea and nausea) in patients with worse outcomes (Shang, et al., 2020). Therefore, a  
393 healthy gut microbiome may support a better immune response to viral infections, thus  
394 inducing an effective protective response to COVID-19. Moreover, the state of this  
395 immune system-microbiota partnership may justify people's susceptibility to infections  
396 and inflammations, which in turn can be associated with a regular diet (Belkaid &  
397 Hand, 2014). A healthy gut or intestinal microbiome is known to be associated with a  
398 diet rich in fibers and a variety of fruits, vegetables, whole grains, legumes, nuts and  
399 seeds, and herbs and spices, as well as a few fermented foods (such as Kefir, *kimchi*  
400 and *sauerkraut*) (Heinen, Ahnen, & Slavin, 2020; Singh, et al., 2017). Thus, the diet  
401 can also assist patients impaired with COVID-19 to recover and improve clinical  
402 outcomes, in addition to being behind lower infection rates or better disease prognosis  
403 (associated with lower mortality and morbidity rates) in certain regions of the planet or  
404 regions with characteristic cuisines or diets.

405 A scheme of the gut-lung connection is depicted in Figure 1. Succinctly,  
406 antigens or microbes in the intestine are 'scrutinized' by Dendritic cells (DC) directly  
407 from the lumen or after translocation through M cells to the GALT (Gut-associated  
408 lymphoid tissue). A combination of microbial cues leads to phenotypic changes in

409 dendritic cells and migration to the draining lymph node. Dendritic cells then induce  
410 the activation of several T cells subsets within the MLN (mesenteric lymph nodes) and  
411 the production of several regulatory cytokines, such as IL-10, TGF- $\beta$ , INF $\gamma$  and IL-6. T  
412 cells then gain immune homing molecules (CCR9, CCR4). As a consequence of the  
413 immune challenge in the respiratory tract, cells activated in the GALT and MLN travel  
414 to the respiratory mucosa via CCR4/6 and induced protective and anti-inflammatory  
415 responses. Additionally, bacterial-derived products (e.g., LPS) can bind to TLR (Toll-  
416 like Receptors) in both intestinal epithelium and macrophages, which results in the  
417 production of several cytokines and chemokines. TLR activation can also encompass  
418 the expression of NF- $\kappa$ B in macrophages. The formation of several bacterial  
419 metabolites (as SCFAs) also affects the gut-lung connection. These products are  
420 conducted to the lung, where they modulate inflammation levels (Samuelson, Welsh, &  
421 Shellito, 2015).

422         The diet-intestinal microbiota and the gut-lung connection have been  
423 extensively reviewed (e.g. (Anand & Mande, 2018; Nurmatov, Devereux, & Sheikh,  
424 2011). It is now widely accepted that food intake affects the intestinal flora (or  
425 microbiota), resulting in bacterial metabolites that modulate immunity, namely by  
426 stimulating immune cells and the movement of sensitized immune cells or metabolites  
427 through the circulatory and lymphatic systems, can reach various distal organs, like the  
428 lungs or the brain. Therefore, unsurprisingly literature on nutrition, respiratory health,  
429 and gut flora increased substantially during the COVID-19 pandemic (Chaari, et al.,  
430 2020; Dhar & Mohanty, 2020). Additional relationships have been established between  
431 dietary-related pre-conditions, such as obesity and severity of COVID-19 infection  
432 (Aoun, et al., 2020). However, the opposite is why some regions or countries have not

433 been as affected by the COVID-19 pandemic as Western countries like Spain or U.S.A.  
434 remain underexplored. Here, we will now focus on the traditional Korean diet and  
435 dietary mechanisms that may target viruses ACE-2 receptors or affect any step of a  
436 virus infection pathway, determining the patient's prognosis. Potential functional foods  
437 commonly used in Korean cuisine will be highlighted for their potential to improve gut-  
438 lung immunity (Table 2).

439 As mentioned above, traditional Korean food is rich in fermented fruits and  
440 vegetables as cabbage. This has already been reported to help mitigate the COVID-19  
441 severity (Bousquet, et al., 2020). It may also be associated with the richness of phenolic  
442 compounds and antioxidants in these foods, as well as with the high levels of  
443 *Lactobacilli* present and ingested upon consumption (Bousquet, et al., 2020; M. K.  
444 Park, et al., 2013). Therefore, the Korean diet has various fronts on which it can offer  
445 better outcomes for patients with COVID-19: high content of important bacteria for a  
446 healthy gut, high levels of antioxidants and phenolic compounds that can act as an anti-  
447 inflammatory and nutritionally rich in whole grains, fibers, and vitamins that further  
448 support a healthy balance for immunity and gut microbiota. In fact, antiviral properties  
449 have already been highlighted in these functional foods, particularly for their immune-  
450 promoting nutraceutical properties, through antioxidation and anti-inflammation  
451 features as summarized by Alkhatib (Alkhatib, 2020).

452 The lung epithelium in the adult is arranged in different types of cells. The  
453 tracheo-bronchial epithelium is a pseudo-stratified layer with ciliated cells and  
454 secretory epithelial cells (Clara), and goblet cells. Human basal cells (potential  
455 epithelial progenitor cells) appear in high numbers below this layer, decreasing as the  
456 lung proceeds into the alveolar space. Neuroendocrine cells may also occur and be

457 innervated by ganglion cells, which are described to regulate cell proliferation and  
458 differentiation. Respiratory bronchioles' structure is not very well described, and these  
459 lead to the alveoli, which are known to be linked mainly by type I and type II alveolar  
460 cells (Camelo, Dunmore, Sleeman, & Clarke, 2014). Therefore, lungs epithelia may  
461 differentiate into different cell types, including types I and II pneumocytes (Figure 2).  
462 Type II pneumocytes make important proteins that reduce the surface tension of the  
463 alveoli, preventing them from collapsing. While type I pneumocytes are thin, flat cells  
464 that grant gas exchange between the alveolus and the surrounding blood capillaries.

465         The SARS-CoV-2 virus can attach and infect alveolar pneumocytes. These  
466 primary human epithelial cells are their ACE-2 receptor, the gateway portal for SARS-  
467 CoV-2, and a different histological structure that may respond differently to virus  
468 infection. Therefore, a potential antiviral that can reduce the virus titer, an  
469 improvement in the survival rate, and a reduction in the rate of symptoms accumulated  
470 from the moment of contagion will be considered beneficial for future medical  
471 applications. This can occur via different pathways or mechanisms, as suggested in  
472 figure 2. An innate immune response against a virus in the respiratory tract is mediated  
473 by recognizing molecular patterns associated with viruses by specific receptors  
474 expressed in epithelial cells.

475         Intake of immunobiotics as yogurts or fermented /preserved foods can induce  
476 resistance and effective immune responses against viruses infection in the respiratory  
477 tract (H. Zelaya, S. Alvarez, H. Kitazawa, & J. Villena, 2016). Moreover, the  
478 respiratory tract also has significant remodeling capacity that can originate in an  
479 aberrant epithelial cell (genetic mutations) or exposure to external irritants and viruses  
480 or cigarette smoke, and this follows similar pathways to those that describe the benefits

481 of immunobiotics (e.g., *Lactobacillus* probiotics) (Camelo, et al., 2014; H. Zelaya, et  
482 al., 2016).

483 The effect of the gut microbiome on the immune response at distal sites or  
484 organs and its effects on the outcome of respiratory infections or disorders is now  
485 increasingly relevant and clear; gut microbiota assists in regulating the antiviral  
486 immunity (Abt, et al., 2012; Ichinohe, et al., 2011), and this has been especially  
487 exposed in infants nutrition (Berni Canani, et al., 2017; Goehring, et al., 2016) and  
488 adults with chronic illness as asthma (Williams, et al., 2016). Potential plant-based  
489 drugs have been continuously screened for their antibacterial, antiviral, anti-cancerous,  
490 and antioxidant activities. More recently, antiviral properties have also been evaluated  
491 as plant-based antiviral natural compounds that may offer less toxicity and may be  
492 coupled with pre-existing therapies, along with improved delivery methods for greater  
493 effectiveness and bioavailability. Common plant compounds include flavonoids,  
494 phenolics, carotenoids, terpenoids, alkaloids, and many others, many of which have  
495 documented antiviral activities (Figure 3).

496 The medical and scientific communities are increasingly interested in  
497 ethnophytotherapeutics, as they offer complementary therapeutic options, with easy  
498 and inexpensive access along with the low potential for toxicity. The traditional Korean  
499 diet is rich in ingredients with a long history of ingredients and elements with strong  
500 antioxidant, anti-inflammatory, antiviral, antibacterial, fat metabolism, and modulating  
501 gut microbiota properties that further support strong respiratory immunity. However,  
502 research on nutraceuticals, plants, and food elements remains inconsistent and very  
503 confusing. Collaborations across several fields, from agriculture to chemistry and  
504 biomedical, will be important to fill the gap. Different comprehensive studies are

505 needed to corroborate and validate associations between consuming a food and the  
506 specific health status or conditions.

507 Moreover, well-planned preclinical, *in vitro* and *in vivo*, and chemical  
508 investigations are still lacking. In controlled feeding trials, validation, as well as small  
509 populations and non-standard evaluation systems hold limitations. Thus, adequate,  
510 comprehensive study designs are required to validate the clinical functions of any  
511 particular food. Additionally, before the COVID-19 pandemic, universal systems were  
512 proposed to study coronavirus-host interaction *in vitro* in an attempt to respond to the  
513 need for identification of antivirals, evaluation of compound toxicity, and viral  
514 inhibition (e.g. (Jonsdottir & Dijkman, 2016)). However, these systems have not been  
515 explored enough when it comes to report the antiviral properties of plants and foods. To  
516 adds up to the current information, recently a clinical practice guideline has also been  
517 developed for the treatment of the SARS-CoV-2 using the Korean herbal medicine (B.-  
518 J. Lee, Lee, Kim, Choi, & Jung, 2020). Further a number of panel discussion has also  
519 been published on the role of the Korean Medicine including the traditional herbal  
520 medicine that includes plant based components for the treatment in the post COVID-19  
521 era (S. Kwon, et al., 2020; Sunju Park, et al., 2020).

#### 522 **4. Chemical Constituents in the Korean Tradition Foods with Antiviral and** 523 **Anti-Respiratory Medicinal Effects**

##### 524 **4.1 Chemical constituents in Kimchi**

525 *Kimchi* is the most widely distributed and popular Korean fermented food,  
526 which is prepared with napa cabbage or the Chinese cabbage or with radish as its main  
527 ingredients (J. K. Patra, Das, & Paramithiotis, 2017). *Kimchi* is prepared by mixing  
528 baechu, radish, powdered red pepper, salt, garlic, ginger, scallion, fermented fish, sugar

529 and flavor enhancers. The addition of all these ingredients enhances the nutritional  
530 value of kimchi by incorporating carotenoids, vitamin C, chlorophyll, capsaicin, sulfur-  
531 containing compounds, phenolic compounds, dietary fiber, and fermentation  
532 metabolites such as lactic acid, glycoproteins, and bacteriocin (J. K. Patra, et al., 2017).  
533 In addition, the literature research states that most of the chemical constituents present  
534 in fermented Korean foods are metabolites of fermentation (Table 3). For instance,  
535 when amino acids are evaluated, most of the measured free amino acids are produced  
536 due to the proteolytic action of microbial enzymes (Jayanta Kumar Patra, et al., 2016).

#### 537 **4.2 Chemical constituents in Chongkukjang, Doenjang, and Gochujang**

538 *Chongkukjang* is a traditional Korean food prepared in rice straw and boiled  
539 soybean fermented with *Bacillus* species rich in polyglutamic acid, isoflavones,  
540 phosphatide, and phenolic acids (H. C. Chang, 2018; N. Y. Kim, Song, Kwon, Kim, &  
541 Heo, 2008). Moreover, D. Y. Kwon, Chung, and Jang (2019) stated that, unlike  
542 *Doenjang* and *Gochujang*, *Chongkukjang* fermentation takes only 2-4 days. Other  
543 reports mention that *Chongkukjang* has anti-inflammatory and antidiabetic properties,  
544 which are partially attributed to the chemical constituents of the soybean and its  
545 fermentative metabolites (D. Y. Kwon, et al., 2019; Wei, et al., 2015). Also, *Doenjang*  
546 is a traditional Korean food made by mixing and fermenting soybeans for about six  
547 months using *Bacillus subtilis*, *Rhizopus* spp., and *Aspergillus* spp. (D. H. Lee, et al.,  
548 2018).

549 Furthermore, *Gochujang* is a Korean traditional fermented food based on a paste  
550 of red pepper-soybean and is commonly used as a sauce in spicy Korean cooking. The  
551 main ingredients of *Gochujang* are red hot pepper powder, waxy rice flour, and  
552 fermented soybean (known as *meju*). *Gochujang* is usually fermented using *Aspergillus*



553 sp. and *Bacillus* sp. strains (J. Y. Cho, et al., 2013). Due to the inclusion of red pepper  
554 and meju, some of the main constituents of *Gochujang* are capsaicin and isoflavones  
555 derivatives. The chemical constituents present in *Chongkukjang*, *Doenjang*, and  
556 *Gochujang* are shown in Table 4.

#### 557 **4.3 Chemical Bioactive Ingredients used in Korean Foods**

558 Some of the most common ingredients in fermented Korean cuisine are napa  
559 cabbage, garlic, and ginger. These ingredients are a rich source of bioactive compounds  
560 like phytochemicals, which are secondary metabolites produced as a defense  
561 mechanism in plants against biotic and abiotic stresses. Some of the most common  
562 phytochemicals found in food-stuff are alkaloids, terpenes, glucosinolates, and phenolic  
563 compounds (Croteau, Kutchan, & Lewis, 2015). Regular intake of these compounds in  
564 the diet has been related to a decreased incidence of non-communicable diseases, and  
565 some have also been used to treat infectious diseases. In this regard, some studies point  
566 to the antiviral potential of some Korean ingredients.

567 For instance, Dong, Farooqui, Leon, and Kelvin (2017) reported that  
568 ginsenosides commonly found in ginseng could interact with a viral hemagglutinin  
569 protein, preventing the attachment of the H1N1 virus to host cells. The chemical  
570 structure of ginsenoside was determined to be crucial as the sugar moieties in these  
571 molecules are pivotal for their bonds with viral hemagglutinin. Moreover, fresh ginger  
572 showed *in vitro* antiviral interest against the human respiratory syncytial virus,  
573 preventing viral attachment and internalization (J. S. Chang, Wang, Yeh, Shieh, &  
574 Chiang, 2013). Some studies also hypothesize that bioactive compounds from garlic  
575 have antiviral properties against influenza A and V, rhinovirus, viral pneumonia, and  
576 rotavirus (Bayan, Koulivand, & Gorji, 2014). Also, obesity, cardiovascular diseases,

577 and diabetes have been described to increase the risk of some respiratory viral diseases.  
578 On this subject, Korean fermented foods have been reported with the potential to  
579 decrease the formation of macrophage foam cells by inhibiting lipid peroxidation  
580 induced by oxidized low-density lipoprotein (Yun, Kim, & Song, 2014). Furthermore,  
581 *in vitro* studies have shown that garlic extracts have antiviral properties against the  
582 influenza A and B virus (P. Mehrbod, E. Amini, & M. J. I. J. o. V. Tavassoti-Kheiri,  
583 2009; Sharma, 2019). It is important to mention that the reported compounds  
584 commonly found in ingredients used in the preparation of traditional Korean fermented  
585 foods go through a lactic acid fermentative process, which metabolizes the compounds  
586 to produce different metabolites. In this sense, some reports state that Korean fermented  
587 foods have potential beneficial health effects, like antiviral potential against the  
588 influenza virus (M.-K. Park et al., 2013), as stated in section 1.

#### 589 **4.3.1 Cabbage**

590 Chinese cabbage or napa cabbage (*Brassica rapa* L.) is used to prepare *Kimchi*,  
591 the most popular fermented Korean food. Chinese cabbage is a rich source of bioactive  
592 compounds, and these constituents may be related to the antioxidant and health-  
593 promoting properties of *Kimchi*. Some of the bioactive constituents most commonly  
594 identified in Chinese cabbage are glucosinolates, carotenoids, tocopherols, sterols,  
595 policosanols. Some of the most common glucosinolates found in Chinese cabbage are  
596 4-hydroxyglucobrassicin, 4-methoxyglucobrassicin, glucoalyssin, glucobrassicinapin,  
597 glucobrassicin, gluconapin, gluconasturtiin, neoglucobrassicin, progotrin, and sinigrin  
598 (Figure 4) (Baek, Jung, Lim, Park, & Kim, 2016). Some of the most commonly  
599 identified bioactive compounds in Chinese cabbage are shown in Table 5.

### 600 4.3.2 Garlic

601 Garlic contains many bioactive compounds, such as organosulfur and phenolic  
602 constituents. Some of them are phenolic compounds, like hydroxybenzoic acid  
603 derivatives, such as gallic and vanillic acid; and hydroxycinnamic acid derivatives,  
604 such as chlorogenic acid, caffeic acid, ferulic acid, p-hydroxybenzoic acid, m-coumaric  
605 acid, o-coumaric acid, p-coumaric acid (Beato, Orgaz, Mansilla, & Montano, 2011; J.  
606 S. Kim, Kang, & Gweon, 2013). Garlic is also the source of flavonoids like the  
607 flavanols catechin, epicatechin, and epigallocatechin gallate; flavonones like quercitrin  
608 and apigenin; flavonols like myricetin, resveratrol, morin, quercetin, and kaempferol  
609 (Figure 5) (J. S. Kim, et al., 2013). Furthermore, one the most important bioactive  
610 compounds identified in garlic is the non-volatile amino acids containing sulfur-like  
611 alliin, allicin, (E)-ajoene, diallyl sulfide, (Z)-ajoene, and 1,2-vinyldithiin (X. N. Lu, et  
612 al., 2011; Martins, Petropoulos, & Ferreira, 2016).

### 613 4.3.3 Ginger

614 Ginger is one of the main ingredients in many food preparations in Korea.  
615 Ginger is a rich source of phytochemicals with potential health-promoting effects.  
616 Some of the main bioactive constituents found in this root are phenolic compounds,  
617 such as gingerols, like 6-gingerol, which is the compound responsible for the pungency  
618 of fresh ginger; while shogaols are the main causes of pungency in dry gingers, and  
619 these compounds are derived from gingerols; some other constituents are zingerone,  
620 paradols like 6-deoxy gingerol and methyl paradols (Figure 6) (Alsherbiny, et al.,  
621 2019). Some other gingerols found in ginger are 8-gingerol, 10-gingerol, 6-shogoal  
622 (Brahmbhatt, Gundala, Asif, Shamsi, & Aneja, 2013). Also, different ginger plants of  
623 the *Boesenbergia* species have phenolic compounds like quercetin, kaempferol, rutin,

624 naringin, hesperidin, caffeic acid, p-coumaric acid, sinapic acid, chlorogenic acid, gallic  
625 acid, luteolin, and diosmin (Jing, Mohamed, Rahmat, & Abu Bakar, 2010). Some  
626 terpenes found in ginger are  $\beta$ -bisabolene,  $\alpha$ -curcumene, zingiberene,  $\alpha$ -farnesene, and  
627  $\beta$ -sesquiphellandrene.

## 628 **5 Pre-clinical and clinical effectiveness in humans**

629 Dietary measures are widely used as adjuvant treatments against influenza  
630 infections. Many fermented foods have antioxidant abilities, which promote the  
631 inhibition of essential enzymes and the disruption of cell membranes, thus avoiding  
632 viral binding and enhancing the capacity of the immune system. As stated in previous  
633 sections, fermented Korean foods are of great value by the multiplicity of  
634 microorganisms with a positive impact on the microbiota (protect the intestinal  
635 mucosa) and confer greater resistance to the immune system – immunobiotics and/or  
636 probiotics. Several microorganisms from fermented foods have been described to  
637 improve human immune response against viral infections (Arena, et al., 2018).  
638 Antiviral effects of lactic acid bacteria (LAB) may be due to increased intestinal barrier  
639 function or stimulation of the immune system through the increase of macrophage  
640 activity and the production of antiviral inhibitory substances ( $H_2O_2$ , organic acids). The  
641 potential of heat-killed *Lactobacillus* probiotics against influenza was highlighted  
642 (Sehee Park, et al., 2018).

643 Patra et al. (Jayanta Kumar Patra, et al., 2016) reviewed many health benefits of  
644 *Kimchi*. Among different pharmacological properties of these foods, namely *Kimchi*,  
645 are their role in modulating the immune system. Activators for the potent transcription  
646 factor Nrf2 (nuclear factor erythroid-2-related factor 2) presented in some fermented  
647 Korean vegetables, as *Kimchi*, are suggested to improve health and metabolism.

648 Fermented cabbage was recently proposed to increase the Nrf2-related antioxidant  
649 effects against COVID-19, modulating the severity of the symptoms and patient  
650 outcomes (Bousquet, et al., 2020). The potential of dietary use of some fermented  
651 foods, probiotics, and prebiotics are being discussed as strategies to promote gut and  
652 upper respiratory tract immunity to better face a possible viral infection as by Sars-  
653 Cov-2, including in patients with COVID-related gastro-intestinal symptoms (Antunes,  
654 Vinderola, Xavier-Santos, & Sivieri, 2020).

655         The *Lactiplantibacillus plantarum* (previously designated *Lactobacillus*  
656 *plantarum*) strain YU (LpYU), originally isolated from traditional Japanese fermented  
657 foods and one of the lactic acid bacteria (LAB) well known for its positive effects on  
658 immune function, was reported to activate Th1 immune responses on mice and prevent  
659 infection by the influenza A virus (A/NWS/33, H1N1) (Kawashima, et al., 2011). In  
660 this work, mice were dosed with 0.011, 0.21, or 2.1mg/day for 14 d, prior to intranasal  
661 inoculation of influenza A virus (IFV). Lungs and bronchoalveolar lavage fluids  
662 (BALFs) were studied to demonstrate that LpYU activated the innate and acquired  
663 immune systems.

664         The intake effects of two Korean traditional fermented soybean products,  
665 *doenjang* and *cheonggukjang*, or a mixture of both, have also been evaluated on the  
666 mice's immune response. However, no antiviral properties were explored in this study  
667 (J. H. Lee, et al., 2017). The conclusion pointed to the increase in humoral and cellular  
668 immunity via Th1 responses in mice fed both products, suggesting an improved  
669 synergic effect. However, the antiviral properties of *Lactiplantibacillus plantarum*  
670 DK119, a microorganism isolated from fermented Korean cabbage, has been studied  
671 against the influenza virus, using a mouse model in a dose and route -dependent way

672 (M. K. Park, et al., 2013). In this study, animals infected with influenza virus were  
673 intranasally or orally exposed to *Lactiplantibacillus plantarum* DK119, which  
674 effectively lowered lung viral loads. The bronchoalveolar lavage fluids from mice  
675 showed elevated concentrations of cytokines IL-12 and IFN- $\gamma$ , and a low degree of  
676 inflammation, which indicates the bacteria's antiviral effects by modulating innate  
677 immunity.

678 Other pre-clinical studies demonstrated the antiviral effects of some  
679 microorganisms from fermented Korean food on the influenza virus. Table 6 displays  
680 some representative studies involving lactic acid bacteria (LAB) isolated from  
681 fermented foods and their immunobiological activity on animal models infected with  
682 the virus under different conditions. The preclinical studies presented in Table 6  
683 demonstrate that the intake of Korean fermented foods, such as kimchi and  
684 Cheonggukjang or even *Lactobacillus* isolated from these foods, improves the immune  
685 system, not only of healthy animals but also in models infected with various types of  
686 virus or with asthma. The microorganisms present in this type of foods can offer  
687 protection for some viral diseases. They have been shown to have protective and  
688 immunomodulatory effects, namely upon regular oral intake of heat-killed forms  
689 isolated from kimchi.

690 As the polyherbal formula Mahwangyounpae-tang (MT), other Korean dietary  
691 supplements have been used to treat respiratory diseases, including asthma (M.-Y.  
692 Park, Choi, Kim, Lee, & Ku, 2010). This supplement, which contains 22 types of  
693 herbal extracts, was orally given to different groups of rats for 28 d at different doses  
694 (800, 400, and 200 mg/kg per day) and showed no significant toxic effects, confirming,  
695 therefore, the safety of these products. Previous studies investigated the

696 pharmacological efficacy for the asthma treatment in mice only using 30 mg/Kg of MT  
697 (Ji Yun Kim, Kim, & Kam, 2003). Also, in humans, Korean fermented foods as *kimchi*  
698 were investigated for potential immune system-stimulating effects (H. Lee, Kim, Lee,  
699 Jang, & Choue, 2014). In this study, healthy college students aged over 20 and having a  
700 body mass index of 18.5-23.0 kg/m<sup>2</sup> took 100 g of *Kimchi* once a day for one month.  
701 However, no significant immunomodulatory effects were detected, possibly due to the  
702 short period of intake of *Kimchi*.

703 Clinical trials involving school-aged children were also conducted by Huang et  
704 al. (Huang, Chie, & Wang, 2018), focusing on the therapeutic impacts of  
705 *Lactocaseibacillus paracasei* (LP), *Limosilactobacillus fermentum* (LF), and the co-  
706 exposure (LP and LF) on asthma, biomarkers of immune function, and fecal microbiota  
707 or flora. These probiotics with well-known immunomodulatory effects were given to  
708 the children for three months. A co-exposure was reported most effective, resulting in  
709 risen peak expiratory flow rates and decreased IgE levels. As Korean fermented foods  
710 are rich in several of these pro- and pre-biotics, it offers a possible  
711 nutraceutical/supplement or functional food value that is yet to be characterized to treat  
712 respiratory disorders and infections, including in children, holding it at their fair safety.  
713 Clinical studies are still few to elucidate better the role of these foods in infections of  
714 the respiratory system.

## 715 **6. Conclusion**

716 Korean traditional foods are widely recognized for their delicious and spicy  
717 flavor, as well as health benefits. One of the most recognized Korean fermented foods  
718 is *Kimchi* (a mixture of fermented vegetables) among others such as *Meju*, *Doenjang*,

719 *Jeotgal*, and *Mekgeolli*, which exhibit several medicinal effects (e.g., anticancer,  
720 antiobesity, antioxidant, anti-inflammatory, antidiabetes) and involve several beneficial  
721 microorganisms (e.g., *Leuconostoc mesenteroides*, *Lactiplantibacillus plantarum*,  
722 *Aspergillus* sp., *Bacillus* sp., *Halomonas* sp., *Kocuria* sp., *Saccharomyces cerevisiae*).  
723 It should be noted that other epidemiological situations caused by the new influenza A  
724 (H1N1) and more recently the pandemic COVID-19, induced by the severe acute  
725 respiratory syndrome coronavirus 2 (SARS-CoV-2), has been devastating, causing  
726 more than 1.21 million deaths worldwide. In addition, edible plants and mushrooms are  
727 used in Korean traditional medicine to treat different health events. The consumption of  
728 traditional Korean foods, such as those fermented by lactic acid bacteria, is recognized  
729 to produce metabolites with antiviral effects against respiratory diseases (e.g., influenza  
730 virus H1N1) by stimulating the immune system. In fact, increased levels of interferons  
731 (INF- $\alpha$  and INF- $\beta$ ) and interleukins (IL-6), in addition to the high secretion of  
732 cytokines IL-2, IL-12 and IFN- $\gamma$  are produced upon, for example, *Lactobacilli* intake.  
733 Adding to this, fermented foods such as *kimchi* and *doenjang* also provide a set of  
734 antioxidants and vitamins (e.g., ascorbic acid), strengthening the immune system and  
735 preventing or modulate allergic reactions such as rhinitis and asthma.

736 The role of gut microbiota on viral infections has been highlighted in the  
737 literature. The gut-lung or axis relationship already reported before the COVID-19  
738 outbreak may predict the patient's prognosis for SARS-CoV-2 infection, particularly  
739 when considering gut symptoms (such as diarrhea and nausea) in patients with worse  
740 outcomes. Thus, the Korean diet, rich in fibers and a variety of vegetables, fruits, whole  
741 grains, nuts and seeds, herbs and spices, and fermented foods (such as Kefir, *kimchi*,  
742 and *sauerkraut*) may lead to a healthy gut microbiome, which may support a better



743 immune response to viral infections, thus inducing an effective protective response to  
744 COVID-19.

745 In addition, plant-based compounds with antiviral properties (e.g., flavonoids,  
746 phenolics, carotenoids, terpenoids, alkaloids, and many others) may aid with an  
747 improved immune response besides the nutritional and medicinal values already well  
748 recognized. Moreover, this type of diet can also help COVID-19 patients to recover and  
749 improve clinical outcomes due to the high levels of antioxidants and phenolic  
750 compounds that further support a healthy balance for immunity and gut microbiota. In  
751 summary, the regular consumption of a healthy diet that includes, e.g., the Korean  
752 functional foods can support human respiratory health, namely via the antiviral  
753 properties of its ingredients, particularly due to their immune-promoting nutraceutical  
754 properties. It has been suggested by the clinical research that the food supplements such  
755 as curcumin and zinc have great potentials in terms of their antiviral activities and thus  
756 these types of food supplements can be useful in the treatment of COVID-19 to boost  
757 the immune system. Although these types of food supplements with their immense  
758 medicinal potentials proves helpful in the treatment of COVID-19, however the food  
759 supplement-drug interaction should be taken into consideration in terms of increasing  
760 toxicity and their drug efficiency. Although much is already known on the properties of  
761 functional foods, well-planned preclinical and clinical studies are required to elucidate  
762 their role in infections of the respiratory tract. In addition, chemical investigations on  
763 the nutraceutical/biomedical properties of both these ingredients and fully prepared  
764 foods may offer a template for improved therapeutics for respiratory infections.

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**773 Conflict of interest**

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775 The authors declare no conflict of interest with the manuscript.

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**778 References**

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1611 **Table 1. Potential beneficial effect of Korean foods against respiratory diseases.**

Korean food	Respiratory and antiviral models	Inhibitory effect	Reference
Chongkukjang extract	Influenza A virus	Neuroraminidase inhibitory effect of 4,565.9 to 28,242.4 by IC <sub>50</sub> (µg/mL).	(Wei, et al., 2015)
Ethanol extract from Cheonggukjang	Allergic asthma in a murine model	70% ethanol extract (100mg kg <sup>-1</sup> day <sup>-1</sup> ) decreased degranulation and histamine release from mast cells	(Bae, et al., 2014a)
<i>L. plantarum</i> <sup>1</sup> (YML009) strain isolated from <i>Kimchi</i>	Influenza H1N1 virus	Antiviral activity at concentrations of 2 <sup>1</sup> - 2 <sup>3</sup> 10x cell-free supernatant.	(Rather, et al., 2015)
<i>L. plantarum</i> <sup>1</sup> DK119 isolated from <i>Kimchi</i>	Influenza H1N1 virus	A 109 CFU/mouse diary dose prevented weight loss of mice and maintained 100% survival.	(M.-K. Park, et al., 2013)
<i>Lactobacillus</i> strains isolated from Korean fermented foods	Mice model	Mice were fed a lyophilized powder (dose of 2.5x10 <sup>10</sup> CFU day <sup>-1</sup> ) and induced the T-lymphocytes proliferation and IFN-γ production	(Won, et al., 2011)
<i>L. citreum</i> <sup>2</sup> HJ-P4 isolated from <i>kimchi</i>	Allergic mice model	A dose of 2x10 <sup>8</sup> CFU/mL enhanced the secretion of IFN-γ and decreased IL-4 and IL-5	(H. Kang, et al., 2009)
<i>L. citreum</i> <sup>2</sup> EFEL2061 isolated from <i>kimchi</i>	Allergic mice model	A dose of 1x10 <sup>10</sup> UFC was given daily and reduced the bystander B cell activation	(Hee Kang, et al., 2016)
<i>S. succinu</i> <sup>3</sup> 14BME20 isolated from <i>doenjang</i>	Allergic asthma in a murine model	A dose of 5x10 <sup>7</sup> UFC reduced cytokines and induced the accumulation of anti-inflammatory cells	(J. Song, et al., 2019)

1612 <sup>1</sup>*Lactiplantibacillus plantarum*; <sup>2</sup>*Leuconostoc citreum*; <sup>3</sup>*Staphylococcus succinus*

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1615 **Table 2. Some functional foods used in Korean traditional cuisine and their**  
 1616 **potential health benefits. Results from a literature survey reporting antiviral**  
 1617 **properties in the food are also indicated.**

<b>Elements used in Korean traditional cuisine</b>	<b>Potential Effects</b>	<b>References</b>	<b>Direct Antiviral evidence</b>
<b>Beet and beet greens</b>	Anti-inflammatory Cholesterol modulation Improve cardiovascular health Immunomodulatory	(Asgary, et al., 2016; Gomes, et al., 2019; Shepherd, et al., 2019; Wylie, et al., 2013)	No
<b>Peppers (genus <i>Capsicum</i>)</b>	Improved fat metabolism / lipemia	(Hobbs, Caso, McMahon, & Nymark, 2014; Y. Lee, Cha, Park, & Lee, 2017; McCrea, et al., 2015)	No
<b>Anchovies</b>	Improve cardiovascular health	(Ferretti, Judd, Taylor, Nair, & Flanagan, 1993)	No
<b>Apples</b>	Improve cardiovascular health Improve fat metabolism	(Bondonno, et al., 2018; Cicero, et al., 2017; Tenore, et al., 2019; Trošt, et al., 2018)	No
<b>Cruciferous vegetables</b>	Antioxidant Anti-inflammatory Modulate GI microbiota	(Kaczmarek, et al., 2019; Kellingray, et al., 2017; López-Chillón, et al., 2019)	Yes (Müller, et al., 2016; Noah, et al., 2014)
<b>Beans, seeds and nuts</b>	Antioxidant Anti-inflammatory	(Hermsdorff, Zulet, Abete, & Martínez, 2011; Nilsson, Johansson, Ekström, & Björck, 2013; Relja, et al., 2017; Reverri, et al., 2015); reviewed in (Bolling, McKay, & Blumberg, 2010; Ganesan & Xu, 2017a; Lorenzon Dos Santos, Quadros, Weschenfelder, Garofallo, & Marcadenti, 2020)	No
<b>Carrots</b>	Antioxidant Cholesterol modulation Modulate GI microbiota Anti-diabetic	(Hu, et al., 2019; Nicolle, et al., 2003)	Yes (Torky, 2013)
<b>Cocoa</b>	Antioxidant	(Cavarretta, et al., 2018; Gu,	No

	Anti-inflammatory Improved fat metabolism Modulate GI microbiota Immunomodulatory	Yu, & Lambert, 2014; S. Jang, et al., 2017; Massot-Cladera, Franch, Castell, & Perez-Cano, 2017; Massot-Cladera, Perez-Berezo, Franch, Castell, & Perez-Cano, 2012; Sarria, et al., 2020)	
<b>Coffee</b>	Antioxidant Improved fat metabolism Anti-inflammatory Immunomodulatory	(Kuang, et al., 2018; Loftfield, et al., 2015; Poole, et al., 2017; Rao & Fuller, 2018; Vitaglione, et al., 2019)	Yes (Tsujimoto, et al., 2010; Tsutomu, et al., 2009; Utsunomiya, et al., 2008); reviewed in (Valentina, 2017)
<b>Garlic and onions</b>	Antioxidant Anti-inflammatory Improved fat metabolism Immunomodulatory	(González-Peña, Checa, de Ancos, Wheelock, & Sánchez-Moreno, 2017; Gonzalez-Pena, et al., 2017; M. Y. Seo, et al., 2019; C. Yang, et al., 2018); Reviewed in (Corzo-Martínez, Corzo, & Villamiel, 2007; S. Bisen & Emerald, 2016)	Yes (J.-B. Lee, et al., 2012; P. Mehrbod, E. Amini, & M. Tavassoti-Kheiri, 2009; Tsai, et al., 1985; N. D. Weber, et al., 1992)
<b>Ginger</b>	Antioxidant Anti-inflammatory Immunomodulatory	(Akhtar, Jantan, Arshad, & Haque, 2019; Jo, et al., 2016; S. Kim, et al., 2018; Motawi, Hamed, Shabana, Hashem, & Aboul Naser, 2011; Tian, et al., 2020); Reviewed in (Anh, et al., 2020)	Yes (Aboubakr, et al., 2016; J. S. Chang, et al., 2013)
<b>Green tea</b>	Antioxidant Anti-inflammatory Improved fat metabolism Immunomodulatory	(Gennaro, et al., 2015; Han, et al., 2016; Newsome, et al., 2014; Yamashita, et al., 2018)	Yes (Cheng, Lin, & Lin, 2002; J.-M. Song, Lee, & Seong, 2005; J. M. Weber, Ruzindana-Umunyana, Imbeault, & Sircar, 2003)
<b>Lentils</b>	Antioxidant Anti-inflammatory Improve cardiovascular health Modulate GI microbiota Improved fat metabolism	(Graf, et al., 2019); Reviewed in (Ganesan & Xu, 2017b)	No
<b>Pumpkin</b>	Antioxidant Anti-inflammatory Improved fat	(Alshammari & Balakrishnan, 2019; Bardaa, et al., 2020; Hossain, et al.,	Yes (Elkholy, Hamza, Masoud, Badr, & El Safty, 2009; Sener, et



	metabolism	2018)	al., 2007)
<b>Tomato</b>	Antioxidant Anti-inflammatory Improve fat metabolism Immunomodulatory	(Schwager, Richard, Mussler, & Raederstorff, 2016; Valderas-Martinez, et al., 2016)	No
<b>Turmeric / curcumin</b>	Antioxidant Anti-inflammatory Improve fat metabolism Modulate GI microbiota	(H. Y. Lee, et al., 2017; H. Y. Lee, et al., 2016; Peterson, et al., 2018); Reviewed in (Labban, 2014; Lobo, Prabhu, Shirwaikar, & Shirwaikar, 2009)	Yes (Anantikulchai, Emprom, Pringproa, & Yamsakul, 2017; Anggakusuma, et al., 2014; Praditya, et al., 2019); Reviewed in (Mathew & Hsu, 2018; Moghadamtousi, et al., 2014)
<b>Yogurt</b>	Antioxidant Anti-inflammatory Improve fat metabolism Modulate GI microbiota Immunomodulatory	(Buendia, et al., 2018; Gonzalez, et al., 2019; Lasker, et al., 2019; Pimentel, et al., 2018; Poutahidis, et al., 2013; Rettedal, Altermann, Roy, & Dalziel, 2019)	Yes (H.-J. Choi, Song, Ahn, Baek, & Kwon, 2009; H.-J. Choi, et al., 2010)

1618 \* Properties reported in pasteurized carrot juice; No- lack of information

1619 **Table 3. Chemical constituents of Kimchi**

Vegetable source	Compounds	References
<i>Kimchi</i> cabbages	Organic acids: acetic acid, citric acid, succinic acid, lactic acid, fumaric acid. Free sugars: fructose, glucose, sucrose, mannitol. Volatile compounds: allyl methyl disulfide, dimethyl trisulfide, diallyl tetrasulfide, 4-ethyl-5-methylthiazole, allyl methyl trisulfide, 3-vinyl-[4H]-1,2-dithin, and 2-phenylethyl isothiocyanate	(Y. J. Choi, et al., 2019)
<i>Kimchi</i> fermented with <i>L. mesenteroides</i> <sup>1</sup>	Lactate, ethanol, acetate, mannitol, diacetyl, acetoin, and 2,3-butanediol	(Byung Hee Chun, Lee, Jeon, Kim, & Jeon, 2017)
<i>Kimchi</i> fermented with red pepper	Glucose, fructose, lactate, acetate, mannitol	(S. H. Jeong, Lee, Jung, Lee, et al., 2013)
Metabolite composition of <i>Kimchi</i> during long-term storage	Decreased levels of free sugars fructose and glucose during storage. Increased levels of lactate, acetate, succinate, gamma-aminobutyric acid, and mannitol.	(S. H. Jeong, Lee, Jung, Choi, & Jeon, 2013)
Metabolic features of	Fermentation metabolites: D-lactate, ethanol,	(S. E. Jeong, et al., 2018)

<i>W. koreensis</i> <sup>2</sup> during Kimchi fermentation	acetate, D-sorbitol, thiamine, folate. Carbohydrates: glucose, mannose, lactose, malate, xylose, arabinose, ribose, N-acetylglucosamine, and gluconate	
Kimchi prepared with napa cabbage and different salts	Volatile metabolites: $\alpha$ -pinene, camphen, myrcene, 1-phellan, dimethyl trisulfide, diallyl disulfide, dipropyl disulfide, 1-butene-4-isothiocyanate, phenethyl isothiocyanate. Nonvolatile metabolites: alanine, valine, proline, serine, threonine, glutamate, phenylalanine, mannitol, tryptophan, stearidonic acid, pinolenic acid, capsaicin, dihydrocapsaicin.	(D. W. Kim, et al., 2017)
Thirteen Korean Kimchi samples from Jeonju	Resveratrol (from the conversion of polydatin into resveratrol by the strain <i>Lactobacillus kimchi</i> JB301), isorhapontigenin, oxyresveratrol.	(Ko, et al., 2014)
Kimchi fermented with <i>L. plantarum</i> <sup>3</sup>	Increased lactic acid levels, glycerol, pyrotartaric acid, pentanedioic acid, 2-keto-1-gluconic acid, ribonic acid, isocitric acid, and palmitic acid.	(S. E. Park, et al., 2016)
Mustard leaf kimchi extracts	Catechin, chlorogenic acid, epicatechin, epigallocatechin gallate, p-coumaric acid, gallic acid, ferulic acid, epicatechin gallate, rutin, catechin gallate, naringin.	(S. Y. Park, et al., 2017)
<i>L. pentosus</i> <sup>4</sup> isolated from Kimchi from Gyeonggi-do, Korea	Ginsenoside Rd, ginsenoside F2, compound K	(Quan, et al., 2010)
<i>L. plantarum</i> <sup>3</sup> HD1 isolated from Kimchi from home, restaurants, and temples located in South Korea	5-oxododecanoic acid, 3-hydroxy decanoic acid, 3-hydroxy-5-dodecanoic acid	(Ryu, Yang, Woo, & Chang, 2014)
Kimchi prepared with different salt contents (0 and 5%)	Lactic acid, acetic acid, xylitol, and fumaric acid.	(S. H. Seo, et al., 2018)

1620 <sup>1</sup>*Leuconostoc mesenteroides*; <sup>2</sup>*Weissella koreensis*; <sup>3</sup>*Lactiplantibacillus plantarum*;

1621 <sup>4</sup>*Lactobacillus pentosus*

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1624 **Table 4. Chemical constituents of *Chongkukjang*, *Doenjang*, and *Gochujang*.**

Vegetable source	Compounds	References
<i>Chongkukjang</i>	Poly- $\gamma$ -glutamic acid	(Ratha & Jhon, 2019)
<i>Chongkukjang</i>	Genistein, daidzein	(N. Y. Kim, et al., 2008)
<i>Doenjang</i> prepared with different content of garlic (2%, 6%, 10%), and thermal processes (heat-drying and freeze-drying)	Essential amino acids: isoleucine, leucine, lysine, methionine, phenylalanine, valine. Non-essential amino acids: arginine, proline, tyrosine, glycine, alanine, serine, glutamic acid, aspartic acid. Non-proteinogenic amino acids: ornithine, o-phosphoserine, taurine, sarcosine, L-citrulline, $\gamma$ -aminobutyric acid, ethanolamine, hydroxylysine.	(Bahuguna, et al., 2019)
<i>Doenjang</i>	Amino acids: glutamate, serine, valine, glycine, leucine, phenylalanine	(B. H. Chun, Kim, Jeong, & Jeon, 2020)
Soybean koji <i>Doenjang</i>	Acids: 2-methylpropanoic acid, acetic acid, 2-methylbutanoic acid, 3-methylbutanoic acid. Alcohols: 3-methylbutan-1-ol, pentan-1-ol. Carbonyls: benzaldehyde, butane-2,3-dione. Phenols: 2-methoxy phenol.	(D. W. Jeong, et al., 2020)
<i>Doenjang</i>	Daidzein, glycitein, genistein	(H. E. Kim & Kim, 2014)
<i>Doenjang</i>	Genistein, daidzein, glycitein, genistein	(M. J. Kim, Kwak, & Kim, 2018)
<i>Doenjang</i>	Apigenin, soyasaponin A2, trihydroxyflavone, luteolin, daidzein, glycitein, genistein, soyasaponin, soyasaponin I, soyasaponin III, soyasaponin $\beta$ g	(S. S. Kim, Kwak, & Kim, 2020)
<i>Doenjang</i>	Daidzein, glycitein, genistein, daidzin- $\beta$ -glucoside, glycitin- $\beta$ -glucoside, genistein- $\beta$ -glucoside, daidzin malonylglucoside, glycitin malonylglucoside, genistein malonylglucoside, daidzin acetylglucoside, glycitin acetylglucoside, genistein acetylglucoside	(Kwak, Son, Chung, & Kwon, 2015)
<i>Doenjang</i> submitted to steaming, drying, meju fermentation, brining, and aging	Isoflavones: malonyldaidzin, malonyglucitin, malonygenistin, acetyldaidzin, acetylglycitin, acetylgenistin, daidzin, glycitin, genistein, daidzein, genistein. Soyasaponins: soyasaponin I-V, soyasaponin $\gamma$ g, soyasaponin $\gamma$ a, soyasaponin Bd, soyasaponin Be	(S. Y. Lee, et al., 2014)

<i>Doenjang</i> and metabolites in rat plasma	Isoflavones: daidzein, genistein, glycitein, malonyl daidzin, malonyl genistein, malonyl glycitin, acetyl daidzin, acetyl genistein, acetyl glycitin. Isoflavone metabolites: 3-hydroxygenistein, hydroxydihydrogenistein, daidzein-4'-glucuronide, daidzein-7-glucuronide, daidzein-4'-sulfate, genistein-4'-glucuronide, genistein-7-glucuronide, genistein diglucuronide, genistein-4'-sulfate, genistein-7-sulfate-4'-glucuronide	(D. H. Lee, et al., 2018)
<i>Gochujang</i> fermented with <i>A. oryzae</i>	Genistein, daidzin, apigenin 7-O- $\beta$ -D-glucopyranoside, quercetin 3-O- $\alpha$ -L-rhamnopyranoside	(J. Y. Cho, et al., 2013)
<i>Gochujang</i>	Capsaicin, dihydrocapsaicin	(Ha, et al., 2010)
Three <i>Gochujang</i> types (white rice, brown rice, and wheat)	Isoflavones: daidzin, genistein, daidzein, glycitein, genistein. Soyasaponins: soyasaponin I-V.	(Y. K. Jang, et al., 2017)
<i>Gochujang</i> prepared with different cereals (wheat, brown rice, and white rice) and peppers ( <i>Capsicum annuum</i> , <i>C. annuum</i> cv. Chung-yang, and <i>C. frutescens</i> )	Apigenin-C-hexoside-C-pentoside, dihydrocapsiate, linoleic ethanolamide, luteolin-C-hexoside, quercetin-O-rhamnoside, dihydrocapsaicin	(G. M. Lee, Suh, Jung, & Lee, 2016)
<i>Gochujang</i> products prepared with combinations of fungal rice koji with <i>B. amyloliquefaciens</i> CJ 3-27 and <i>B. amyloliquefaciens</i> CJ 14-6	Genistein, acetylgenistin, daidzin, luteolin-diglucoside, genistein, apigenin-diglucoside, apigenin-glucoside, isovitexin-glucoside, daidzein, glycitein, luteolin, hydroxydaidzein, capsaicin, dihydrocapsaicin	(Shin, et al., 2016)

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1626 **Table 5. Metabolites with potential health-promoting effects in Chinese cabbage**1627 **used in the preparation of traditional Korean foods.**

Sample	Identified compounds	Method of identification	References
Chinese cabbage	Glucosinolates: progoitrin, sinigrin, glucoalyssin, gluconapin, glucobrassicinapin, glucoeurucin, glucocochlearin, 4-hydroxyglucobrassicin, glucobrassicin, 4-	LC-qTOF-MS	(Baek, et al., 2016)

	methoxyglucobrassicin, neoglucobrassicin, gluconasturtiin. Carotenoids: violaxanthin, antheraxanthin, lutein, $\alpha$ -carotene, $\beta$ -carotene, chlorophyll.		
Hairy roots of Chinese cabbage induced by CuO nanoparticles	Glucosinolates: gluconasturtiin, glucobrassicin, 4-methoxyglucobrassicin, neoglucobrassicin, 4-hydroxyglucobrassicin, glucoallysin, glucobrassicinapin, sinigrin, progoitrin, and gluconapin. Hydroxycinnamic acids: p-hydroxybenzoic acid, protocatechuic acid, syringic acid, gentisic acid, vanillin. Hydroxycinnamic acids: p-coumaric acid, ferulic acid, chlorogenic acid, t-cinnamic acid. Flavonols: myricetin, quercetin, kaempferol, catechin, naringenin, rutin, hesperidin.	UHPLC and UHPLC-TQMS	(Chung, Rekha, Rajakumar, & Thiruvengadam, 2018)
Non-heading Chinese cabbage	Phenolic compounds: kaempferol-O-sophoroside-O-hexoside, kaempferol-dihexoside, kaempferol-sophoroside, kaempferol hexoside, myricetin-O-arabinoside, ferulic acid, quinic acid, protocatechuoyl hexose	UPLC-MS	(Managa, Remize, Garcia, & Sivakumar, 2019)
Chinese cabbage sprouts	Aliphatic glucosinolates: progoitrin, sinigrin, glucoallysin, gluconapin, glucobrassicinapin. Indolic glucosinolates: 4-hydroxyglucobrassicin, glucobrassicin, 4-methoxyglucobrassicin, neoglucobrassicin	HPLC-DAD	(Samec, Pavlovic, Redovnikovic, & Salopek-Sondi, 2018)
Chinese cabbage (leaves and roots)	Glucosinolates: glucobrassicin, 4-methoxy glucobrassicin, neoglucobrassicin	HPLC	(Zang, et al., 2015)
Chinese cabbage	Glucosinolates: glucoallysin, sinigrin, progoitrin, gluconapin, glucobrassicinapin, gluconasturtin, glucobrassicin, 4-methoxyglucobrassicin, neoglucobrassicin, 4-hydroxyglucobrassicin	UPLC	(Thiruvengadam, Kim, & Chung, 2015)

1628 **Abbreviations:** HPLC - High Performance Liquid Chromatography; HPLC-DAD - high-  
1629 performance liquid chromatography with a diode-array detector LC-qTOF-MS - liquid chromatography  
1630 in combination with hybrid quadrupole time-of-  
1631 flight mass spectrometry; UPLC - ultra performance liquid chromatography; UPLC-MS - Ultra  
1632 performance liquid chromatography - tandem mass spectrometer; UHPLC-TQMS - ultra-high  
1633 performance liquid chromatography coupled with a triple quadrupole mass spectrometry.

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1636 **Table. 6 Pre-clinical studies on the effects of microorganisms from Korean**  
 1637 **fermented foods on laboratory animal models. Abbreviations: BALFs -**  
 1638 **bronchoalveolar lavage fluids; CGJ - *Cheonggukjang*; EPS - exopolysaccharides;**  
 1639 **IAV - influenza A virus; IFV- influenza virus; i.p. intraperitoneal; nF1 - heat-**  
 1640 **killed *Lactiplantibacillus plantarum*; OVA - ovalbumin; MLD50 - 50% mouse**  
 1641 **lethal dose; CFU - colony-forming unit; FFU – fan filter unit; IFN- $\alpha$  - interferon**  
 1642 **alpha; IgA – immunoglobulin A antibody; PFU – plaque-forming unit.**

Aims	Animal model	Exposure route	Evaluated Parameters	Dosing and period	Main Results	Reference
Evaluate <i>L. brevis</i> <sup>1</sup> KB290 impacts against influenza virus infection in mice	Mice	Oral		Lyophilized KB290 suspended in PBS for 14 days and then intranasally infected with 50% mouse lethal dose of IFV	<i>L. brevis</i> <sup>1</sup> alleviated clinical symptoms, by production of IFN- $\alpha$ and increase of IFV-specific IgA production	(Waki, et al., 2014)
Evaluate if pretreatment of mice with <i>L. plantarum</i> <sup>2</sup> from the fermented Korean cabbage can increase protection against influenza virus infection	Mice	Intranasal or oral exposure	BALFs and lungs	Animals were treated once with (107 CFU / mouse) of <i>L. plantarum</i> DK119 strain (, 4 days prior infection with a lethal dose of influenza virus	<i>L. plantarum</i> <sup>2</sup> showed to be a beneficial probiotic against influenza virus infection by intranasal or oral exposure	(M. K. Park, et al., 2013)
Evaluate the therapeutic effect of CGJ on a mouse model of ovalbumin (OVA)-induced asthma by the suppression of histamine release	Mice	I.p.	BALFs, lungs	After sensitized by i.p. of OVA and then turned with OVA inhalation, animals were administered i.p. ethanol-extracted CGJ (100mg/kg/day) for 16 days.	Efficacy of CGJEs as a dietary therapy of histamine-mediated allergic diseases, probably by inhibition of mast cell activation.	(Bae, Shin, See, Chai, & Shon, 2014b)
Evaluate the health benefits of regular oral intake of nF1 against influenza virus infection	Mice	Oral		Daily oral intake (10 mg) of nF1 for 14 days followed by intranasally MLD50 of influenza A and B viruses, and the	Daily oral intake of nF1 delayed death of infected mice; increased survival rates	(Sehee Park, et al., 2018)

				same feeding regimen for 14 days		
Evaluate anti-rotavirus activity by the bacterial supernatant, lysate, and the EPS from <i>L. plantarum</i> <sup>2</sup>	Mice	Oral	Blood, heart, and small intestine	EPS (1 mg/mouse) for 2 days prior and 5 days after pups infection with the murine rotavirus epidemic diarrhea (10 µL of 2 × 10 <sup>4</sup> FFU)	Decreased the duration of diarrhea, limited epithelial lesions, reduced rotavirus replication in the small intestine, and better animal recovery by EPS	(K. Kim, et al., 2018)
Evaluate the immunostimulatory effects of <i>L. bulgaricus</i> <sup>3</sup> on the OSV-induced suppression of local and systemic humoral immunity in mice infected with IAV	Mice	Oral	BALFs, lungs	Daily single oral dose of 400 µL of <i>L. bulgaricus</i> <sup>3</sup> for 35 days. On d22, intranasal infection with 0.5 pfu IAV; followed by oral 50 µg of OSV in 100 µL of 5% methylcellulose (MC) as a vehicle or MC alone, twice daily	Regular intake of <i>L. bulgaricus</i> <sup>3</sup> can stimulate humoral immunity of anti-PR8-specific S-IgA and IgG in BALF and anti-PR8-specific IgG and IgA in serum against IAV infection	(Takahashi, Sawabuchi, Kimoto, Sakai, & Kido, 2019)
Evaluate if <i>S. succinus</i> <sup>4</sup> from doenjang normalises immune response and benefits allergic diseases	Mice	Oral	BALFs, lung, mediastinal lymph nodes, mesenchymal lymph nodes and spleen	<i>S. succinus</i> <sup>4</sup> (5 × 10 <sup>7</sup> CFU/ mouse) every other day to day 20, then sensitized and replaced by ovalbumin as an allergen	Therapeutic potential for allergic asthma, due to suppression of airway inflammation by increase in Treg (regulatory T cells) responses	(T. S. Kim, Song, Lim, Lee, & Lee, 2019)

1643 <sup>1</sup>*Levilactobacillus brevis*; <sup>2</sup>*Lactiplantibacillus plantarum*; <sup>3</sup>*Lactobacillus bulgaricus*;

1644 <sup>4</sup>*Staphylococcus succinus*

1645

1646 **Figure legends**

1647 **Figure 1 - Potential connection between the gut-lung axis and nutrition related to**

1648 **the host-defense by the intestinal microbiota and lung immunity.** Adopted from

1649 Samuelson et al. (Samuelson, et al., 2015). The gastrointestinal tract (GI) or gut and

1650 lungs influence their homeostasis reciprocally. The unbalanced gut microbiota is

1651 correlated with lung disorders and infections. For example, antibiotic abuse can

1652 cause changes in the structure of the microbial intestinal community structure,

1653 which can result in altered immunity and changes in microbial growth conditions

1654 and, in turn, cause respiratory responses; or in the other way, a viral infection or

1655 inhalation of antigens/pathogens can alter immunity and microbial communities,

1656 resulting in changes in the gut. SCFAs, short-chain fatty acids; LPS,

1657 lipopolysaccharide; DC-T cells, Dendritic cell-T cell. Some of the intervenient

1658 immunity cells include: IL-6 (interleukin-6), IFN  $\gamma$  (interferon-gamma) and TNF- $\alpha$

1659 (Tumour Necrosis Factor alpha), as well as migrating immune and DC-T cells,

1660 CCR 4/6 (Chemokine Receptor 4/6), CD4+ (Cluster of Differentiation antigen 4)

1661 and Th1 (T-Helper Cell type 1) that are carried in the circulatory vessels.

1662 **Figure 2 – Focused effects of gut or gastrointestinal microbiome in lung immunity.**

1663 Adopted from Camelo et al. (Camelo, et al., 2014) and Zelaya et al. (Hortensia

1664 Zelaya, Susana Alvarez, Haruki Kitazawa, & Julio Villena, 2016).

1665 **Figure 3 - Classification of phytochemicals used as antivirals.** Reproduced from

1666 Ghildiyal et al. (Ghildiyal, Prakash, Chaudhary, Gupta, & Gabrani, 2020), under the

1667 PMC Open Access Subset for unrestricted research re-use and secondary analysis in

1668 any form or by any means with acknowledgement of the original source (originally

1669 Fig. 1).

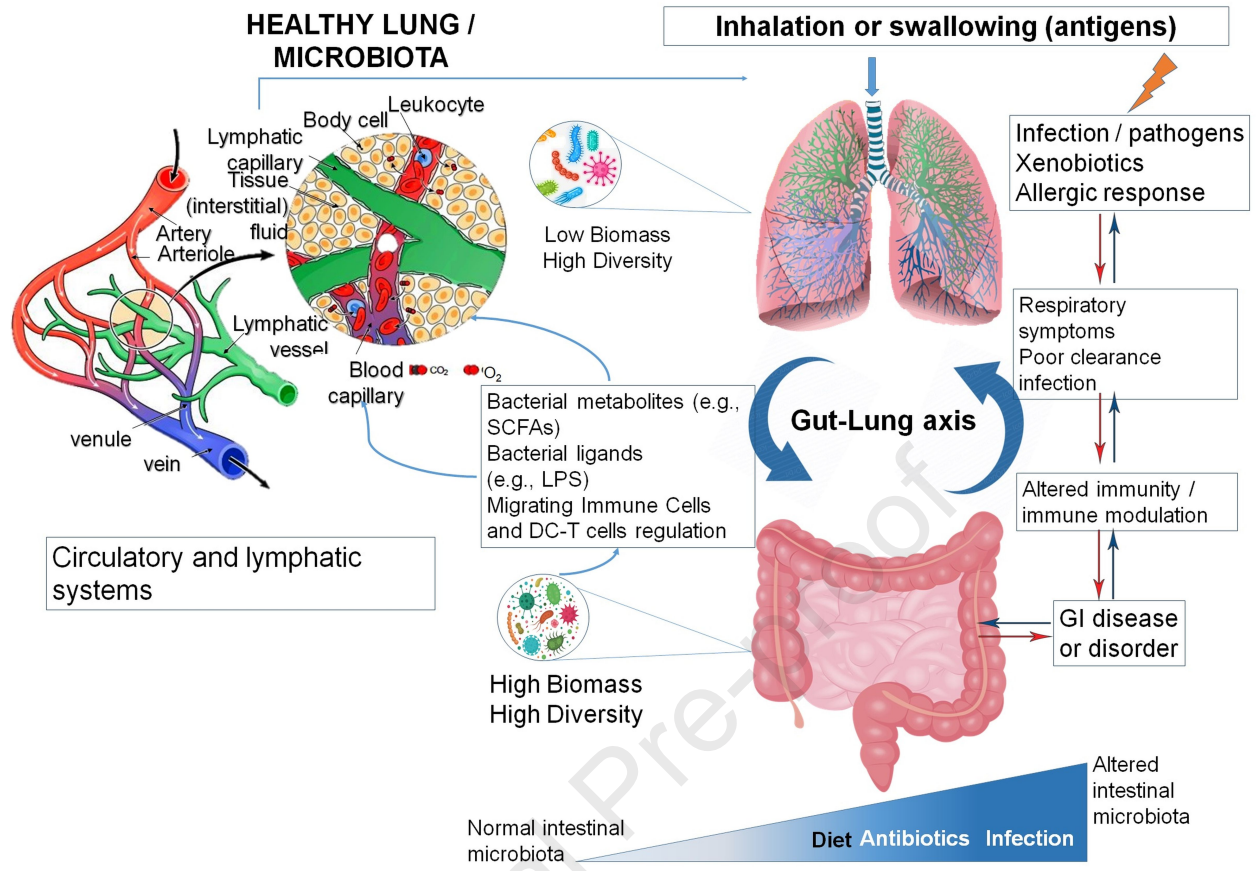
1670 **Figure 4. Glucosinolates commonly found in Chinese cabbage.** a) 4-  
1671 hydroxyglucobrassicin, b) 4-methoxyglucobrassicin, c) glucoalyssin, d)  
1672 glucobrassicinapin, e) glucobrassicin, f) gluconapin, g) gluconasturtiin, h)  
1673 neoglucobrassicin, i) progoitrin, j) sinigrin

1674 **Figure 5. Graphical representation of some bioactive compounds in garlic:** a) (Z)-  
1675 ajoene, b) ajoene, c) diallyl sulfide, d) allicin

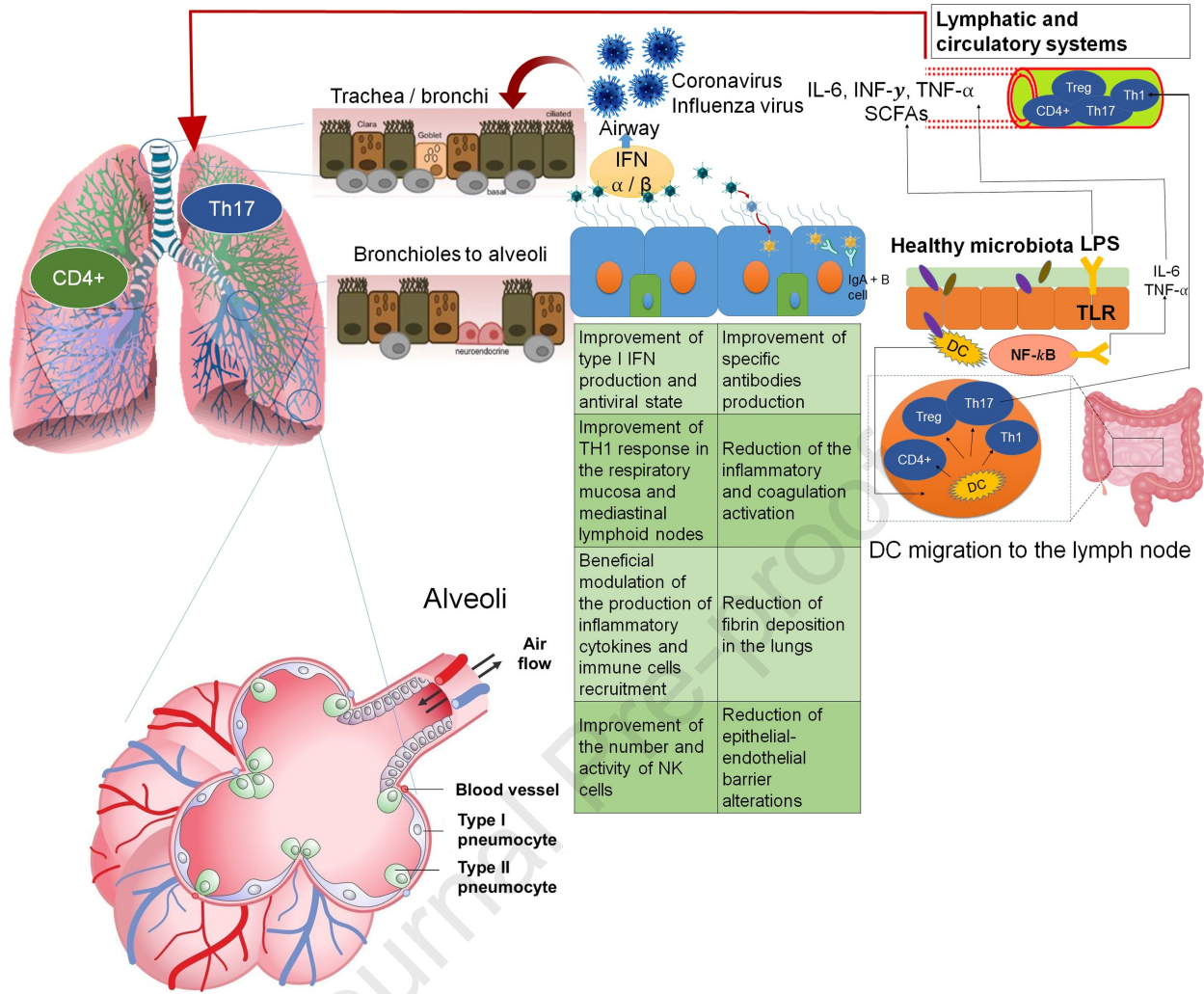
1676 **Figure 6. Graphical representation of some bioactive compounds found in ginger:**  
1677 a) gingerol, b) zingerone, c) hesperidin, d) naringin.

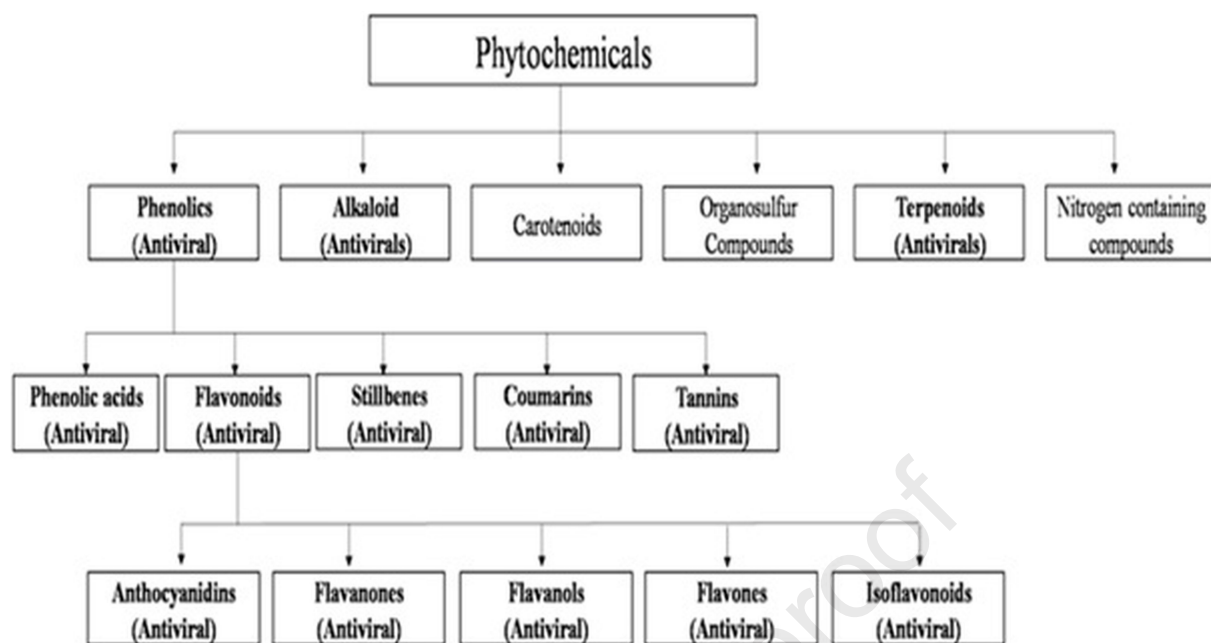
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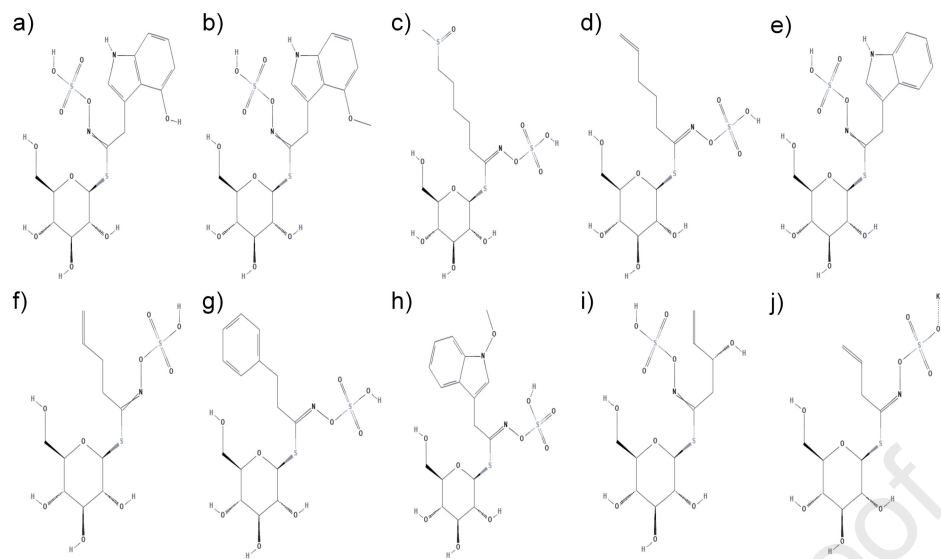






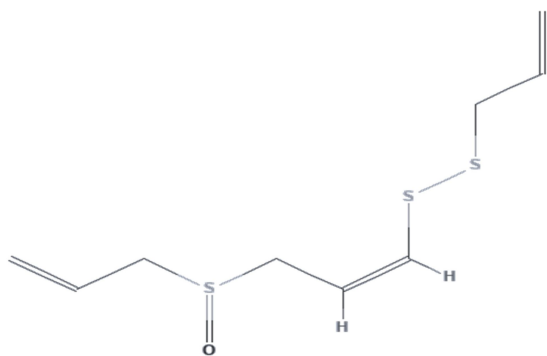




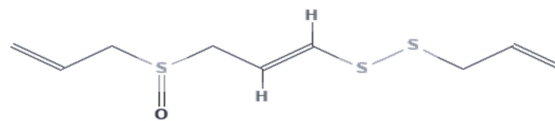


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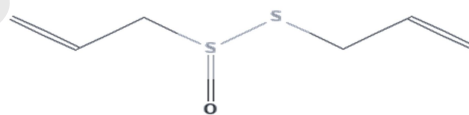
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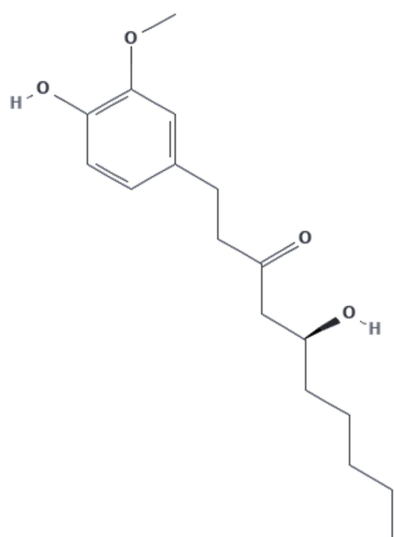
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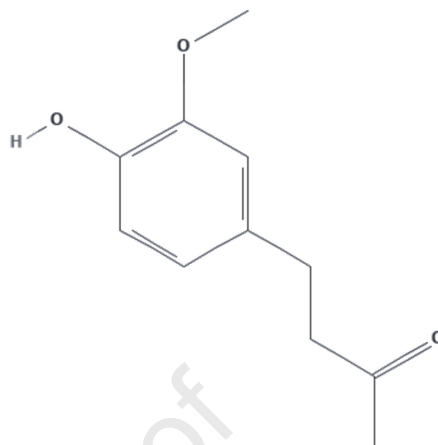
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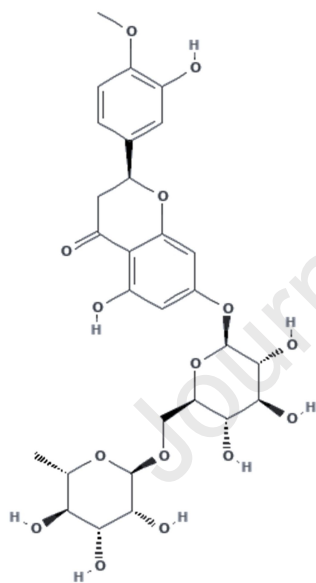
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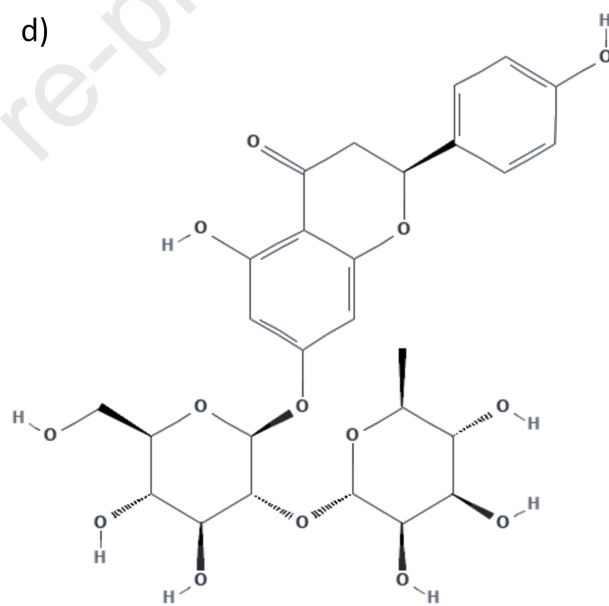
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d)



**Highlights**

- KTF is based on healthy food that balances disease prevention/treatment.
- KTF outline their multiple medicinal effects and support strong respiratory immunity.
- Potential functional foods used in KTF are highlighted for their potential to improve gut-lung immunity.
- Regular oral intake of bioactive ingredients used in KTF offer protection for viral diseases.
- Through protective and immunomodulatory effects, as evidenced in pre-clinical and clinical studies.