



Efficacy of Garlic and Onion against virus

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ABSTRACT

In the current scenario, pharmaceutical industry is dependent on chemical based drugs to treat viral infection. However, these drugs are known to induce many side effects in human body. There is pressing need to promote safe alternative to chemical based antiviral drugs. Onion and garlic are natural sources which are known to possess antiviral properties. It is well known that onion and garlic are rich source of organosulfur compounds. Organosulfur compounds like quercetin and allicin are associated with inhibition of viral infection. These chemicals can hinder virus attachment to host cell, alter transcription and translation of viral genome in host cell and also affect viral assembly. Quercetin can affect entry and attachment of Enterovirus and Influenza virus on host cell. This compound also has ability to inhibit RNA polymerase which is necessary for viral replication. Quercetin also inhibit process by which virus alter signalling pathway in host cell. Organosulfur compounds like allicin, diallyl trisulfide and ajoene are main chemicals which impart antiviral property to garlic. It is known that allicin can pass through phospholipid membrane of cell and can further contribute in inhibiting viral multiplication. Considering numerous studies which corroborate antiviral effect of onion and garlic, this paper recommends consumption of these plants as a safe alternative to prevent virus infection.

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INTRODUCTION

Garlic (*Allium sativum*) and onion (*Allium cepa*) are highly valuable for medicinal significance. According to (FAO, 2019), worldwide production of onion and garlic is 97.8 million tons and 28.16 million tons, respectively. China and India are the main producers of onion and garlic worldwide. The Republic of Korea, Egypt, and the United States of America

are also countries involved in producing garlic (FAO, 2019). The United States, Turkey, and Iran are the main onion producing countries. Garlic is also cultivated in Russia, Myanmar, Spain, Bangladesh, and Ukraine (FAO, 2019). Production of garlic and onion has continuously increased in the past decade. This escalation in the production of these plants can be attributed to the dietary and therapeutic properties of these plants.

Allium sativum and *Allium cepa* have been recognized for their medicinal value since ancient time period. Oldest document Egyptian Code Ebers has mentioned *Allium* to be valuable for treating heart problems, cancer, and other diseases (Fenwick *et al.*, 1985). Healing significance of *Allium* species was also emphasized by Hippocrates and Pliny the Elder. The medicinal importance of garlic has been mentioned in the oldest report, Ebers Papyrus, from Egypt (Block, 1985). The Father of Ayurvedic medicine, Charak, has also mentioned the importance of onion in maintaining blood fluidity and

strengthening the heart (Chutani and Bordia, 1981). Application of onion extracts are known to cure eye disorders, dog bites (Fenwick *et al.*, 1985) and prevent cancer cell growth (Corzomartinez *et al.*, 2007). Similarly, garlic intake is considered as a natural remedy to treat parasite infection, esophagus infections, digestive problems, and fungal diseases (Rivlin, 2001). Apart from medicinal benefits, onion and garlic have a strong smell and provide peculiar taste to food (Yayeh *et al.*, 2017).

The medicinal property of the *Allium* species is linked with the presence of organosulfur compounds. The present review is an attempt to analyze recent studies on phytochemicals of onion and garlic. This review also provides insight on the efficacy of *Allium cepa* and *Allium sativum* in control of viral infection.

Phytochemicals in Garlic and Onion

Both garlic and onion contain a high amount of water, carbohydrates, and fibers. Garlic consists of 58.58% water, whereas water content in onion is 89.11%. (Table 1). Garlic and onion have a high amount of carbohydrates. While garlic comprises of 33.06% carbohydrate, onion bulb possesses 9.34% carbohydrate. The amount of dietary fibre in garlic and onion are 2.1% and 1.7%, respectively. A small amount of monounsaturated and polyunsaturated fatty acids are also present in garlic and onion. Both garlic and onion have a good amount of flavonols and organosulfur compounds which impart medicinal property to these plants. Table 1 represents nutritional composition of garlic and onion (USDA, 2019)

Garlic and Onion contains flavonoids such as anthocyanins and flavanols (Slimestad *et al.*, 2007). The anthocyanins are responsible for the red/purple colour of the bulb, whereas flavanols like quercetin and its derivatives provide yellow and brown skins of many other varieties of these plants (Rodrigues *et al.*, 2017). Isorhamnetin, Kaempferol Myricetin, and Quercetin are flavanols present in these plants (USDA, 2019). The amount of Quercetin is more as compared to other flavanols. Table 2 indicates the amount of flavanols in 100g of garlic and onion (USDA, 2019).

Organosulfur compounds play an important role in imparting medicinal value to garlic and onion. Garlic is rich in organosulfur compound alliin (S-allylcysteine sulfoxide) (Amagase, 2006). Enzyme alliinase can convert alliin into allicin. It has been observed that the flavor of garlic is associated with allicin. Allicin can be further converted into diallyl sulfide, diallyl disulfide, diallyl trisulfide, and diallyl tertasulfide. Abiotic factors like temperature and

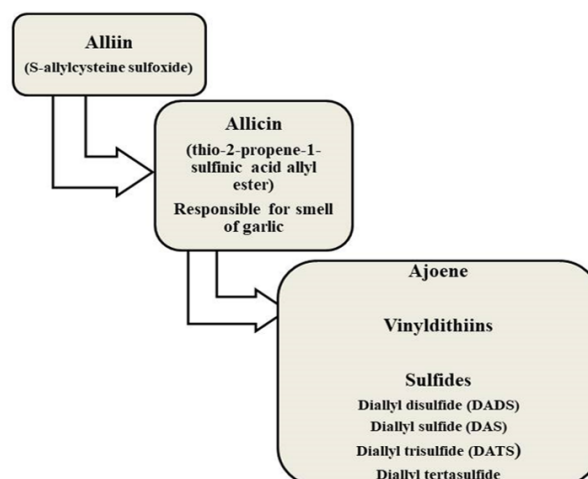


Figure 1: Illustration to show organosulfur compounds and their conversion process in garlic

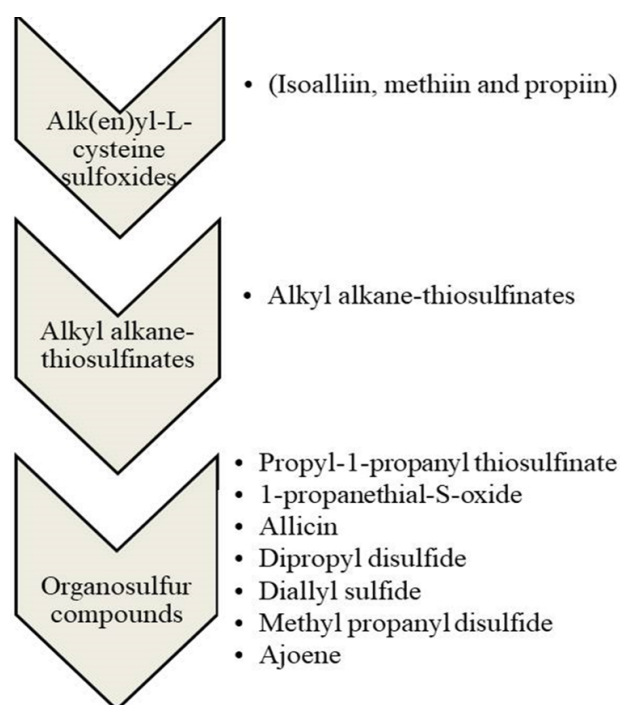


Figure 2: Illustration to show conversion process of organosulfur compounds in onion

time as important in determining the concentration of these sulfur compounds in garlic (Brodnitz *et al.*, 1971). Allicin and other organosulfur compounds are correlated with the medicinal significance of garlic (Iciek *et al.*, 2009). Figure 1 depicts the conversion process of various organosulfur compounds present in garlic.

Onion bulb contains (+)-S-alk(en)yl-L-cysteine sulfoxide and γ -glutamyl peptide cysteine in a high amount. These compounds are responsible for 70% of the total sulfur in onion (Lawson, 1996). Isoalliin, methiin, and propiin are three main non-volatile

Table 1: Nutritional composition of garlic and onion

Nutrient	Unit	Value per 100g in garlic	Value per 100g in onion
Water	g	58.58	89.11
Protein	g	6.36	1.1
Total lipid	g	0.50	0.10
Carbohydrates	g	33.06	9.34
Fibres, total dietary	g	2.1	1.7
Sugars	g	1	4.24
Fatty acids, total saturated	g	0.089	0.042
Fatty acids, total polyunsaturated	g	0.249	0.017
Fatty acids, total monounsaturated	g	0.011	0.013

Table 2: Flavonols present in 100g of raw garlic and onion

Flavonols	Amount (mg/100g) in garlic	Amount (mg/100g) in onion
Isorhamnetin	0	5
Kaempferol	0.3	0.7
Quercetin	1.7	20.3
Myricetin	1.6	0

Table 3: Effect of garlic on virus

Virus name	Effect	References
Common cold virus	Decrease	(Josling, 2001)
Coxsackie B1 virus	No effect	(Tsai <i>et al.</i> , 1985)
Cytomegalovirus	Decrease	(Meng <i>et al.</i> , 1993; Nai-Lan <i>et al.</i> , 1993)
Dengue virus	Decrease	(Hall <i>et al.</i> , 2017)
Herpes simplex 1	Decrease	(Tsai <i>et al.</i> , 1985)
Herpes simplex 2	Decrease	(Weber <i>et al.</i> , 1992)
HIV	Decrease	(Shoji <i>et al.</i> , 1993; Tatarintsev <i>et al.</i> , 1992)
Infectious Bronchitis virus	Decrease	(Shojai <i>et al.</i> , 2016)
Influenza A virus	Decrease	(Fenwick <i>et al.</i> , 1985)
Influenza B virus	Decrease	(Fenwick <i>et al.</i> , 1985)
Newcastle Disease virus	Decrease	(Harazem <i>et al.</i> , 2019)
Potato Virus Y	Decrease	(Mohamed, 2010)

and odorless alk(en)yl cysteine sulfoxides in onion bulb. Isoalliin is the main alk(en)yl cysteine sulfoxides, which accounts for more than 80% of the total amount of alk(en)yl cysteine sulfoxides. Methiin and propiin are present in low amounts in onion (Jones, 2004). Enzyme alliinase catalyze reaction for the conversion of the alk(en)yl-L-cysteine sulfoxides into compounds, like alkyl alkane-thiosulfinates. These alkyl alkane-thiosulfinates impart characteristic taste to *Allium*. These unstable alkyl alkane-thiosulfinates are further transformed into other organosulfur compounds, including allicin, dipropyl

disulfide, diallyl sulfide, propyl-1-propanyl thio-sulfinate, 1-propanethial-S-oxide, methyl propanyl disulfide, and ajoene. Apart from the conversion of alk(en)yl cysteine sulfoxides, γ -glutamyl cysteine is also transformed into different organosulfur compounds like S-allyl cysteine and S-allyl mercaptocysteine in onion (Block, 1985). Figure 2 indicates organosulfur compounds and their conversion in onion.

Garlic is known to possess organic selenium compounds and steroidal saponins (Lanzotti, 2006). These chemicals have the potential to reduce the

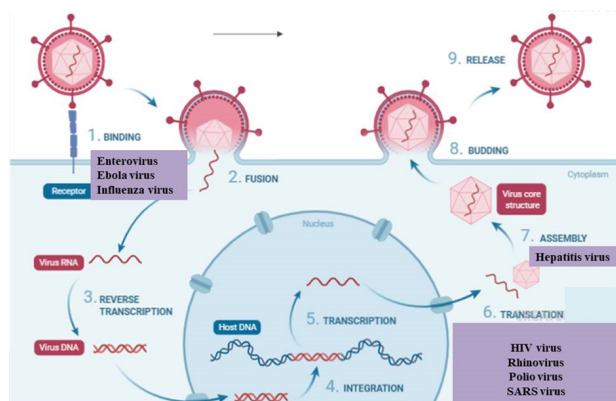


Figure 3: Mechanism of quercetin in host cell

growth of cancer cells (Arnault and Auger, 2006). Many selenium compounds like γ -glutamyl-Se-methylselenocysteine and Se-methylselenocysteine are present in garlic. Onion and garlic contain a high amount of carbohydrates. Onion has a high amount of non-structural and soluble carbohydrates, which form a substantial part of onion dry matter. These include monosaccharides (glucose, fructose, and sucrose) and fructooligosaccharides (FOS) (Darbyshire and Henry, 1979, 1981).

Effect of Garlic and Onion on virus

Flavonoids present in onion and garlic have a strong inhibitory effect on virus multiplication. Phytochemicals present in these plants have been observed to block the formation of protein and genetic material in the virus (Castrillo and Carrasco, 1987; Vrijssen *et al.*, 1987; Zandi *et al.*, 2011).

Onion contains quercetin and kaempferol as main flavanols. These compounds have been found to affect the growth of many viruses (Kumar and Pandey, 2013). Onion extracts were effective in decreasing infection of New Castle Disease virus by blocking of the attachment of the virus with the cell (Harazem *et al.*, 2019). Both garlic and onion were observed to exhibit strong antiviral activity (Chen *et al.*, 2011). Similarly, onion and garlic were observed to reduce infection of Potato virus Y, which is known to severely affect the yield of potato crop (Mohamed, 2010). This antiviral property in onion was found to be associated with quercetin, zalcitabine, allicin, and ribavirin (Chen *et al.*, 2011).

Garlic is also considered to possess strong antiviral properties. For example, experiments have proved that garlic extract can minimize influenza A and B viral infections (Fenwick *et al.*, 1985). Similarly, garlic is effective against cytomegalovirus (Meng *et al.*, 1993; Nai-Lan *et al.*, 1993), rhinovirus, HIV, herpes simplex virus 1 (Tsai *et al.*, 1985), herpes simplex virus 2 (Weber *et al.*, 1992), viral pneumonia,

and rotavirus. However, Coxsackie B1 virus was not affected with the addition of garlic extracts (Tsai *et al.*, 1985). In another study, garlic was observed to significantly minimize the occurrence of the common cold virus (Josling, 2001). Garlic exhibited strong inhibitory effects against the multiplication of the Infectious Bronchitis Virus (IBV), which affect the poultry industry (Shojai *et al.*, 2016).

Chemicals like Ajoene, allyl alcohol, and diallyl disulfide in garlic can act against HIV infected cells (Shoji *et al.*, 1993; Tatarintsev *et al.*, 1992). Organosulfur compounds like allicin, diallyl trisulfide, and ajoene are the main chemicals which impart antiviral property to garlic (Hughes *et al.*, 1989; Weber *et al.*, 1992). In an experimental study, compounds like diallyl disulfide (DADS), diallyl sulfide (DAS), and alliin considerably reduced inflammation during dengue virus infection (Hall *et al.*, 2017). It was observed that these chemicals affected the oxidative stress response mechanism (Hall *et al.*, 2017).

Onion and Garlic are, therefore, important plants which could be used as an alternative treatment for viral infection and for the prevention of severe disease development. Table 3 summarizes the effect of garlic on the different virus.

Mechanism of action against virus

It is a challenge for medical science to combat viral diseases. One of the main challenges in treating viral diseases is the development of resistance in the virus against the antiviral drugs. The high mutation rate of viral RNA polymerase enhances the development of this resistance in virus with RNA genome (Elena and Sanjuan, 2005). With fast mutation in genome of the virus, any antiviral drug proves to be ineffective in a short time (Bolken and Hruby, 2008). Moreover, these antiviral drugs can affect the human body by inducing side effects (Bindu and Anusha, 2011). Therefore it is necessary to find a natural source for inhibiting viral infection.

Viruses require several enzymes for replication. Viruses are dependent on cellular machinery for various replication processes. Anti-viral drugs generally target the process of virus cycle like attachment, uncoating, replication of genetic material, translation, and release. Quercetin is the main compound present in onion, which is associated with an anti-infective and anti-replicative effect on the virus. Many researchers have conducted a study to elucidate the mechanism of quercetin action against viruses. The effectiveness of Quercetin is associated with the ability of this chemical to target cellular processes during virus infection. Quercetin is known for its ability to prevent viral entry or inhibiting components required for viral replication.

Quercetin is known to be an effective compound against viruses like poliovirus, Hepatitis viruses, influenza type A virus (IAV) (Castrillo and Carrasco, 1987). Since onion is a rich source of quercetin, therefore onion can be utilized to minimize viral infection.

Virus entry is considered as the first step of the viral multiplication cycle. Therefore inhibition of this step can minimize viral infectivity (Dimitrov, 2004). Quercetin is well-known to act against the entry of the virus in the host cell. For example, Hemagglutinin and neuraminidase are envelope glycoproteins responsible for entry of the Influenza virus (Takimoto *et al.*, 2002). This glycoprotein helps in attachment and membrane fusion of the virus to the host cell (Takimoto *et al.*, 2002). The process of membrane fusion further facilitates the release of the viral ribonucleic proteins into the cytosol (Takimoto *et al.*, 2002). Ribonucleic protein is then transported into the nucleus, which is the site for genome replication (Takimoto *et al.*, 2002). In an interesting study, quercetin was observed to interact with Haemagglutinin protein, which resulted in the inhibition of virus entry into the cell (Wu *et al.*, 2016). Similarly, quercetin reduced Enterovirus infection by blocking viral attachment stage of viral infection (Yao *et al.*, 2018). In another study, Quercetin 3-O-D-glucoside, a derivative of quercetin, was demonstrated to target the entry of Ebola virus in the host cell (Qiu *et al.*, 2016).

Many studies have reported an inhibitory effect on quercetin on viral replication. Many studies have proved that quercetin can affect viral replication by many ways. For example, quercetin derivative have been proved to inhibit the translation of polio-virus RNA (Castrillo and Carrasco, 1987). The process of formation of multiple copies of polio-virus using the minus-RNA strand was blocked by quercetin (Castrillo and Carrasco, 1987). This was attributed to a reduction in viral RNA Polymerase, an enzyme essential to initiate the formation of the viral genome. Similarly, quercetin was observed to inhibit the translation process of the hepatitis C virus (Gonzalez *et al.*, 2009). SARS-CoV protease, which is required for multiplication of the SARS virus, was inhibited in the presence of quercetin (Chen *et al.*, 2006). Scientists have also observed that quercetin derivatives can increase zinc uptake, which can inhibit RNA Polymerase (Hung *et al.*, 2002; Krenn *et al.*, 2005; Sreenivasulu *et al.*, 2010). Another interesting study suggests that quercetin can induce mitochondrial biogenesis in a host cell, which could further minimize susceptibility to influenza A virus infection (Davis *et al.*, 2008; Nieman *et al.*, 2010). Quercetin inhib-

ited the Human Immunodeficiency Virus-1 integrase and reverse transcriptase enzymes in HIV infected cell (Fesen *et al.*, 1993; Tanaka *et al.*, 2009). Quercetin also has the potential to disrupt the activation of RNA polymerase by reducing the processing of polyprotein by Rhinovirus proteases (Hellen *et al.*, 1989).

Quercetin is also known to affect cytokines in the host cell. Cytokines are a group of proteins secreted by cells of the immune system such as macrophages, B and T lymphocytes, endothelial cells, etc. These cytokines act as chemical messengers in cell signaling pathways. Quercetin is able to change proinflammatory cytokine activities in dengue virus-infected cells (Das *et al.*, 2018). Some authors also believe that the presence of quercetin could increase phosphorylation of eukaryotic initiation factor (eIF2 α) in response to virus infection and thereby prevent viral replication. Therefore the application of quercetin is efficient in enhancing the immune response in the host cells. It has been observed that during the replication process, RNA viruses, including Rhinovirus release protease which attack host cells by cleaving eukaryotic initiation factor (eIF)-4GI and eIF4GII. This ultimately blocks cap-dependent host cell protein synthesis and therefore facilitates viral multiplication (Glaser and Skern, 2000; Gradi *et al.*, 2003). Quercetin has the ability to reduce the cleavage of eIF4II and minimize the formation of viral capsid protein. This affects the replication of Rhinovirus replication (Ganesan *et al.*, 2012).

Apart from viral entry and viral replication, quercetin has a strong potential to inhibit the assembly of new progeny virus in the host cells. For example, quercetin reduced the activity of Heat Shock Protein involved in translation and assembly of the Hepatitis virus (Gonzalez *et al.*, 2009; Rojas *et al.*, 2016). Figure 3 summarizes the effect of quercetin on virus entry, replication, and assembly. Mechanism of quercetin in host cell: Virus infection include (1) Attachment of virus on host cell membrane (2) Virus entry in host cell (3) Reverse transcription (4) Replication of virus genetic material (5)transcription (6) Translation (7) Viral assembly. Quercetin can prevent attachment of virus-like Influenza virus, Ebola, and Enterovirus. Quercetin affects the signaling pathway in the host cell. Quercetin can inhibit the process of transcription or translation in a virus like HIV, Rhinovirus, Poliovirus, SARS virus, which then obstructs virus multiplication. Quercetin can affect the assembly of viral envelop, which thereby block the formation of new progeny viruses.

As quercetin plays an important role in imparting

antiviral property to onion, similarly, allicin is the chemical present in garlic, which acts against the virus. More research studies are needed to elucidate the mechanism of action of allicin on the viral life cycle. It is known that allicin can pass through the phospholipid membrane of the cell and can further contribute in inhibiting viral multiplication. Few authors have identified methods by which allicin and garlic inhibit viral infection, but these methods are more focused on changes in host cell machinery. Allicin can modulate the immune system in response to viral infection. It has been proved that allicin can block the release of pro-inflammatory cytokines such as IL-6 and tumor necrosis factor- α (TNF- α) (Shin *et al.*, 2013; Gu *et al.*, 2013). This suppression of cytokines was also corroborated in an experimental study on Reticuloendotheliosis virus-infected cells (Wang *et al.*, 2017). Apart from inhibiting cytokines, allicin has a property to alter transcription of the nuclear factor kappa B (NF- κ B) and DNA binding activity. It can also block the expression of NF- κ B-mediated inflammatory target genes (Ban *et al.*, 2007). Allicin has a high amount of selenium and sulfur, which impart antioxidant effect by reacting with intracellular thiol compounds (Pandurangan *et al.*, 2015).

CONCLUSIONS

The present paper provides insight into the antiviral role of onion and garlic. Onion and garlic have been observed to inhibit diverse viruses. Organosulfur compounds present in onion and garlic are responsible for affecting different stages of the virus cycle. Quercetin is one of the most prominent organosulfur compounds present in onion. Quercetin can affect entry and attachment of the Enterovirus and Influenza virus on the host cell. This compound also has the ability to inhibit RNA polymerase, which is necessary for viral replication. Replication has been affected in a wide range of viruses like poliovirus, SARS virus, and HIV. Quercetin also inhibits the process by which virus alter signaling pathways in the host cell. Since onion is a natural source of quercetin, therefore it should be further explored to develop an effective drug against the virus. Despite considerable research on the antiviral property of onion and garlic, many questions are still unanswered. Therefore more detailed study should be conducted to elucidate a complete mechanism of action of onion and garlic against the virus. Also, more clinical trials are needed to analyse the antiviral property of these plants.

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