Outbreak of Coronavirus Disease 2019 (Covid-19) in India and Consideration of Preventive Aspects by Ayurveda

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ABSTRACT

In December 2019, an outbreak of severe acute respiratory syndrome Coronavirus (SARS-CoV-2) infection occurred in Wuhan city, Hubei Province, China (East Asia) furthermore worldwide including India. On 30 January 2020, the first case of the COVID-19 pandemic was reported in India. India has reached more than 1.5 lakh confirmed cases including more than 4000 fatalities by dreadful COVID-19 infection. At present, there is no vaccine for prevention or medicine for treatment. Only preventive measures like frequently hand-wash by soap and water, or hand sanitizers along with social distancing are effective to avoid the exposure of this virus. Ayurveda is the oldest acknowledged organized medicine on the earth. Immunity has an important role in maintaining health and prevention of diseases. In Ayurveda, Rasayana drugs are known for their immunomodulation and rejuvenation properties. On March 31, 2020, Ministry of AYUSH has issued advisory for enhancing immunity through lifestyle modification, dietary management, prophylactic interventions and simple remedies based on the symptoms. After that successful implementation, Government of India has planned to conduct clinical trials on three herbal nootropic and immunomodulatory drugs viz. Ashwagandha, Guduchi and Mulethi and AYUSH-64 (Ayurvedic anti-malaria drug) for their preventive properties against Covid-19 infections. This review article covers summary of the COVID-19 i.e. transmission, clinical presentation, investigation and prevention along with preventive measures in according to Ayurveda that can be adopted for future clinical trial.

INTRODUCTION

Coronaviruses (CoVs) have a single stranded RNA genome with a helical symmetry which is covered by an enveloped structure. Size of Coronaviruses ranges between 26.2 and 31.7 kilobases (kb) which is the largest size for RNA viruses. The name of Corona for virus is derived from Latin corona word which means "crown", due to its crown like spikes presentation over the surface of virus under microscope (Dogra et al., 2020). Coronaviruses belong to the Coronaviridae family and have three dissimilar genera: alpha, beta and gamma in which alpha-
and beta Coronaviruses (CoVs) are widely spread in humans and bats, which cause mild respiratory infections. However, two beta Coronaviruses causing SARS-CoV emerged in China in 2002 and MERS-CoV emerged in Arabia (UAE) in 2012 were responsible for prevalent epidemics (WHO, 2020b). In December 2019 Novel Coronavirus 19 erupted in the Wuhan City, Hubei province in China country (East Asia). Origin of this virus is still controversial but as said by Chinese media the Huanan Seafood Wholesale Market of Wuhan city is source which is famous for consumption of seafood and unusual creatures like bats, snakes etc. The medical system of China recognized this new Coronavirus as Severe acute respiratory syndrome (SARS)-CoV-2 by the International Committee on Taxonomy of Viruses (ICTV) (Gorbalenya et al., 2020). The World Health Organization declared this disease as pandemic on 11th March 2020. Now coronavirus disease (COVID-19) has spread to many countries and Territories around the world. Worldwide total confirmed cases are 6,700,000 and have 394,875 fatalities as on 5th June, 2020. As per the Ministry of Health and Family Welfare’s latest data released on Saturday 5th June, total number of cases in India has risen up to 2,36,657 including 115,942 active cases, 114,072 cured/discharged/migrated, 6,642 fatalities and single day jump is 9887 which is highest till date (MOHFW, 2020c). In present scenario, there is no any specific vaccine to prevent or antiviral drug for the treatment of Covid-19 associated pathologies. According to WHO approximately 4 billion people (80%) of the world, currently depend on herbal medicine for some aspect of primary health care. For any circumstances prevention from diseases is better than cure, so modulation of immune responses by different measures may be useful in reducing disease aggravation and mortality rate (Chaturvedi et al., 2020).

In Ayurveda, Rasayana drugs are known for their immunomodulation and rejuvenation properties, which are considered to play important role in Covid-19 management. Several experimental and clinical studies have demonstrated immunomodulatory effects of Rasayana drugs such as Ashwagandha (Withania somnifera), Guduchi (Tinospora cordifolia), and Amalaki (Emblica officinalis) and many other drugs of Ayurveda (Ziauddin et al., 1996).

Aim and Objective

The main aim of this review article is to describe in detail about coronavirus disease (COVID-19) in India and preventive measures by Ayurveda along with their possible mechanism.

Structure of Corona Viruses

The RNA genome of Coronavirus is packed in the nucleocapsid protein and further covered with envolops. Main important structural proteins of Coronavirus are spike (S) protein (trimeric), membrane protein (M), envelop protein (E), and nucleocapsid protein (N). The RNA genome of Coronavirus has seven genes that are arranged in specific sequence (Figure 1) (Guo et al., 2008)

Transmission

The virus that causes COVID-19 is mainly transmitted by droplet transmission contact transmission and aerosol transmission. Droplet transmission occurs when respiratory droplets (when the droplet particles are >5-10 μm in diameter) containing viruses produced from coughs or sneezes of infected person. Contact transmission occurs when a healthy person comes in contact with contaminated surface and then touches mouth, nose, or eyes by same hand. (Liu et al., 2020). SARS-CoV-2 is stable for up to 1 day on cardboard, 2-3 days on plastic and steel and up to three hours in aerosols. Therefore, it is potential to get infected by touching contaminated objects or through the air. It can also spread through sweat, stool, urine, and respiratory secretions. The incubation period for Covid-19 is from 2-14 days, with an average around 5.2 days. The incubation period for any disease is the time duration between infections and manifestation of symptoms. Infectivity index can be measured by using R0 (reproduction number or reproductive ratio) and in case of COVID-19 it is approximately from 2.7-4.2 (Li et al., 2020).

Recent Studies show that COVID-19 in children is less common than adults because children have elevated angiotensin-converting enzyme 2 (ACE2) and lymphocyte count, suffer numerous viral infec-
tions and recent BCG immunizations, which may boost their both innate and adaptive immunity (Wu and McGoogan, 2020). COVID-19 positive pregnant woman can transmit the virus to her fetus or neonate by vertical transmission is still unknown.

Clinical features

According to Indian Council of Medical Research (ICMR), New Delhi, 69% of the confirmed cases during testing in India were found to be asymptomatic. Common clinical features of COVID-19 can include fever (99%), dry cough (60%), myalgia (44%), fatigue (70%) and dyspnea but in advanced stages, infection can cause pneumonia, acute respiratory distress syndrome (ARDS), kidney failure and even death (Guan et al., 2020).

Investigations

Early diagnosis of COVID-19 is essential for the isolation of confirmed cases to prevent further transmission in society. Some common lab investigations among COVID-19 patients are normal or decreased WBC count, decreased lymphocyte count (60%), elevated C reactive protein (CRP) due to inflammation, high lactate dehydrogenase and elevated D-dimer which is similar as seen in SARS-CoV and MERS-CoV infections. On chest imaging bilateral patchy shadows and ground-glass opacities (GGO) are seen (Mardani et al., 2020). A nasopharyngeal (NP) swab and/or an oropharyngeal (OP) swab are often recommended for screening or diagnosis of early infection COVID-19. Within 5 to 6 days of the onset of symptoms, patients with COVID-19 have demonstrated high viral loads in their upper and lower respiratory tracts. Nasopharyngeal (NP) swab has become the preferred swab as it is tolerated better by the patient, safe to operate. SARS-CoV-2 RNA was detected in only 32% of OP swabs, which was significantly lower than the level in nasal swabs (63%). At present confirmation of cases of COVID-19 is based on the unique sequences of viral RNA by nucleic acid amplification tests (NAAT) such as real-time reverse transcriptase polymerase chain reactions (RT-PCR) with confirmation by nucleic acid sequencing.

Trial Treatment

In present scenario, no specific virus target based drug or vaccine is available for COVID-19. The current therapy for Covid-19 involves only symptomatic treatment and supportive care along with prevention of complications. Now many drugs have been tried for treatment of COVID-19 that includes anti-malarial drug hydroxychloroquine (HCQ), convalescent plasma therapy, BCG vaccination and several antiviral drugs such as remdesivir, lopinavir etc. HCQ is considered as a remedy for COVID-19 treatment due to its immuno-modulatory, anti-inflammatory, anti-viral effects and reducing viral replication rate. For the protection of high-risk individuals, ICMR, New Delhi, has recommended a protocol for prophylaxis use of HCQ for COVID-19 infection (MOHFW, 2020b). Convalescent plasma therapy is based on plasma of a patient who has recovered from COVID-19 contains specific antibodies which have ability to fight against SARS-CoV-2 infection. According to researches this is passive immunization and it can be used as preventive measure and for treatment in severe cases but chance of subsequent re-infection is more with therapy. It needs more extensive randomized controlled trials to assess the effectiveness of the therapy. In developing countries like India, BCG (Bacille Calmette-Guerrin) vaccination is given to generally all the infants in the first few days of life for prevention of severe forms of tuberculosis. This vaccine may have great connection to increased nonspecific immunity. When any infant immunized with BCG then live attenuated bacteria enter in the body, replicating and stimulating the non-specific effects on the immune system. When any other infection enters in body that is not even TB, they might respond more robustly manner. WHO has compared the incidence of COVID-19 cases in countries where the BCG vaccine is given in vaccination schedule and where it is not given and result is very amazing that less cases of COVID-19 are reported in countries where BCG vaccine has been given in neonatal/infantile age. Now many clinical trials are registered for the effects of BCG vaccination given to health care workers but in the absence of evidence, WHO did not recommend BCG vaccination for the prevention of COVID-19 (WHO, 2020a).

Precautions

Till date, no drug or vaccine is developed for prevention and treatment of COVID-19 so it will be better to take preventive steps. COVID-19 is mainly transmitted by respiratory droplets and physical contact so it is essential to practice precautionary measures to prevent transmission. Standard precautions consist of hand hygiene by alcohol-based hand rubs (ABHRs), Hand washing with soap and water at least for 20 seconds, Awareness should be done on importance of social distancing (maintain a distance of 1-1.5 meters), necessity of wearing medical masks (NIOSH-certified N95 or equivalent) and avoidance of touching eyes, mouth, or nose. (MOHFW, 2020a). Government of India has requested to endorse use of “Aarogya Setu mobile application” for information, risk alert and relevant advisories against COVID-19. On May5, 2020 Uttar Pradesh (UP) government
Table 1: General Measures for enhance immunity

| AYUSH Advisory | Scientific Aspects |
|----------------|--------------------|
| a) Drink warm water throughout the day | 1. Warm water is an excellent natural medication for cold, cough, sore throat and nasal congestion. It dissolves phlegm and removes it from respiratory tract and builds up immune system of the body  
2. *Acharya Vagbhata* has mentioned that hot water improves digestive power and good for throat diseases. It is indicated in hiccup, *Vata* and *Kapha* disorders, acute fever, cough, running nose, dyspnoea and pain in flank. |
| b) Yogasana, Pranayama and Meditation for at least 30 minutes in a day. | 1. *Yogasana, Pranayama* (breathing techniques) and *Meditation* work as a holistic fitness package. *Yogasana* improves mental strength, physical strength by down-regulation of the hypothalamic pituitary adrenal (HPA) axis and the sympathetic nervous system. *Yoga* improves immunity by drainage of lymph (a viscous fluid rich in immune cells) which helps the lymphatic system to fight against infection.  
2. *Pranayama* (breathing techniques) improves blood circulation and provides more *Prana* (oxygen) to the various parts of the body and also improves the power of respiratory muscles  
3. *Meditation* increases production of serotonin that improves mood, immune system and energy level of the body. *Meditation* lowers the levels of blood lactate which reduces tendency of anxiety attacks (Gowda, 2017). |
| c) *Haldi* (Turmeric), *Jeera* (Cumin), *Dhaniya* (Coriander) and *Lahasun* (Garlic) in cooking. | 1. Curcumin is the main active component of *Haldi* (*Curcuma longa*) and it is also responsible for its yellow color. Researchers have proved that Curcumin provides both innate and adaptive immunity by modulating immune cells. Curcumin provides immunomodulatory effects by neutrophils, macrophages, monocytes, natural killer cells (NK cells) etc. Curcumin also have antioxidant and anti-inflammatory effect (Srivastava et al., 2011)  
2. *Jeera* (*Cuminum cyminum*) is a good source of vitamin A, C, iron, potassium and minerals which boosts immune system and it is very rich in antioxidants, fights with free radicals and afterward lowers the risk of infections.  
3. *Lahasun* (*Allium sativum*) is used for prevention and treatment of common cold. *Lahasun* (*Allium sativum*) is effective in reduction of blood pressure in hypertensive patients but it does not reduce lipoprotein level in blood which is a biomarker of atherosclerosis (Esmail and Al-Snafi, 2016)  
4. *Coriander* (*Coriandrum sativum*) possesses anti-microbial, antioxidant, diuretic, anti-diabetic, anti-convulsant and anti-helminthic and anti-mutagenic activity. |

has launched “Ayush Kavach app” which provides updates for measures to enhance immunity based on natural resources and Ayurveda.

**Prevention of COVID-19 by Ayurveda**

The body’s immune system is most effective weapon in people to fight against COVID-19. Good nutrition, exercise and proper sleep are three important pillars which is extremely necessary for improving the immune system in human. *Ayurveda* propagates the contributions of nature in maintaining health and improving immunity. *Ayurveda* recommends local and systemic prophylaxis trial for respiratory diseases that may be useful in COVID-19 prevention. On the basis of Ayurvedic literature, scientific publications and recommendation by eminent *Vaidyas* ministry of AYUSH has advised the self-care guidelines on 31 March 2020 for protective health measures and boosting immunity especially for respiratory health. The advisory of AYUSH neither has claimed effective treatment for Corona virus nor any specific drug to combat for COVID 19. All the sugges-
Table 2: Ayurvedic Immunity Promoting Measures

| AYUSH Advisory | Scientific Aspects |
|----------------|--------------------|
| a) Chyavanprash (10gm) in the morning | 1. *Chyavanprash* is an Ayurvedic health tonic described in the *Charaka Samhita*. It is a polyherbal *Avaleha* which has 50 medicinal herbs and their extracts which is used to endorse health and prevent diseases.  
2) Main ingredient of *Chyavanprash* is *Aamalaki* (*Emblica officinalis*) which is rich source of vitamin C. *Acharya Charak* has described that *Aamalaki* is the best rejuvenating herbs (*Pandey and Chaturvedi, 2005*) and useful in relieving cough and skin diseases  
3) Main function of *Chyavanprash* is to maintain health and improves the immune system of the body. Clinical studies have suggested that *Chyavanprash* has anti allergic activity, improves immunity; pulmonary function test (PFT), Natural killer (NK) cell activity and increases phagocytic activity (*Sastry et al., 2011*) |
| b) Herbal tea or decoction made from *Tulsi* (Basil), *Dalchini* (Cinnamon), *Kalimirch* (Black pepper), *Shunthi* (Dry Ginger) and *Munakka* (Raisin) - once or twice a day. | 1) Tulsi (*Ocimum sanctum Linn*) has anti-bacterial, anti-viral and anti-fungal activity.  
2) A decoction of the leaves of Tulsi (*Ocimum sanctum Linn*) is very effective for the treatment of respiratory disorders (bronchitis, asthma, influenza, cough and cold) (*Kumar et al., 2010a*)  
3) Researchers have proved that Black pepper (*Piper nigrum*) has immuno-modulatory, anti-inflammatory, anti-oxidant and anti-microbial activity.  
4) Dalchini (*Cinnamomum zeylanicum*) has antioxidant, antimicrobial, anti-inflammatory, anti-cancer, and anti-diabetic property.  
5) *Shunthi* (*Zingiber officinale*) has anti-inflammatory, anti-platelet aggregation, antimicrobial, anti-fungal and anti-rhinovirus activity. The main ingredient of fresh ginger is beta-sesquiphellandrene which is effective against Rhinovirus and many bacterial infections.  
6) *Munakka* (Raisin) have cough suppressant activity so it is effective in management of dry cough and due to its soothing property *Munakka* (Raisin) reduces irritation in the throat.  
7) *Munakka* (Raisin) fights against the free radicals and have antioxidants, anti-inflammatory and antimicrobial properties (*Rekik et al., 2016*). |
| c) Golden milk once or twice a day. (Half tea spoon *Haldi* powder mixed in 150 ml hot milk) | 1) Golden milk is very effective in boosting up of immunity because both milk and turmeric are powerful antioxidant, detoxification agent, anti-inflammatory and having immuno-modulatory properties. |
Table 3: Ayurvedic Procedures

| AYUSH Advisory | Scientific Aspect |
|----------------|-------------------|
| a) Pratimarsh Nasya by sesame oil / coconut oil or Ghee in morning and evening. | 1) Pratimarsh Nasya is administration of oil through the nostrils in dose of 2 drops morning and evening. It can be given daily and even in all the seasons. 2) Drug of Nasya Karma (sesame oil / coconut oil or Ghee) may be absorbed by receptor cells of olfactory mucosa, sensory receptors of trigeminal nerve and cavernous sinus. It helps in removal of morbid Dosha and maintains equilibrium. |
| b) Oil pulling therapy once or twice a day by 1 tsf sesame or coconut oil in mouth. (Do not drink, Swish in the mouth for 2 to 3 minutes and spit it followed by warm water rinse) | 1) Oil pulling therapy is a potent detoxifying technique that is mentioned in the Charaka Samhita as a Kavala or Gandusha. Oil pulling therapy purifies the entire system by oil gargling because tongue is connected to different organ such as kidneys, lungs, liver, heart etc. 2) The sesame plant (Sesamum indicum) contains several kinds of sesame lignans which has antifungal activity. Polyunsaturated fatty acids present in sesame oil reduces free radical injury occurring in oral cavity (Anand et al., 2008). |

Table 4: During dry cough / Sore throat

| AYUSH Advisory | Support of Ayurvedic literature and scientific Publications. |
|----------------|----------------------------------------------------------|
| a) Steam inhalation with fresh Pudina leaves (Mint) or Ajwain (Caraway seeds) by once in a day. | 1) Steam inhalation is very useful for respiratory system disorders. Mint oil is widely used essential oil and its main ingredients are menthol and iso-menthone. It helps in boosting the immune response and has anti-inflammatory, anti-microbial and analgesic property. 2) Chewing Ajwain seeds (Trachyspermum ammi) with lukewarm water is very effective for cough, cold and clearing nasal blockage by discharging the mucus easily (Rajan et al., 2011). |
| b) Lavanga (Clove) powder mixed with natural sugar / honey can be taken 2-3 times a day in case of cough or throat irritation | 1) Researchers have established that honey has immunoglobulin, vitamins and iron in large quantity. Regular use of honey strengthens the white blood corpuscles to battle against bacterial and viral infections (Kumar et al., 2010b). 2) Clove showed antiviral activity against Herpes Simplex virus and other viruses due to eugenin constituent isolated from clove buds. Clove possesses antimicrobial, anti-oxidant, anti-fungal properties and is one of the Nature’s premier antiseptic. |

Future researches in Ayurveda concerns to COVID 19

Ayurveda has potential to save millions of lives from SARS-CoV-2 infection by enhancing host defence and immune homeostasis. In Ayurveda, Rasayana therapy is known for their immunomodulation and rejuvenation properties, which are important in prevention and treatment of Covid-19. The Ministry of AYUSH has released its independent advisory to public for self-care measures, which has received a wholehearted response. The Ayurveda has received better government support after the establishment of the Ministry of AYUSH. For validation of Ayurvedic formulation, against Covid-19, the AYUSH Ministry and Council of Scientific and Industrial Research (CSIR) has started collaborative work on four Ayush formulations. These formulations are Ashwagandha, Yashthimadhu (Mulethi), Guduchi + Pippali and AYUSH-64. Competitive study is also plan between Hydroxychloroquine and Ashwagandha for high-risk population.
Ashwagandha (Withania somnifera)

Ashwagandha may be beneficial in providing antiviral immunity by increasing Interferon-gamma (IFN-gamma responses) and anti-inflammatory activities by decreasing the quantity of Interleukin -1, Interleukin -6 and Tumor necrosis factor which are the main factors related for COVID-19. Ashwagandha may be an effective agent in the management of COVID-19 infection by modulation of host Th-1/Th-2 immunity (Patwardhan et al., 2020).

Guduchi (Tinospora cordifolia)

The major phytocomponents reported in Guduchi are tinosporine, diterpenoid Cordifolioside-A etc. Cordifolioside-A has reported to acquire immunomodulatory activity and enhances innate immunity against COVID-19 infections. Tinosporin, diterpenoid has very effective anti-viral property especially for the treatment of retroviruses and other viral diseases (Akhtar, 2010).

Mulethi (Glycyrrhiza Glabra)

The major phytocomponents reported in Mulethi (Yashtimadhu) is glycyrrhizin which is very effective in inhibiting replication of the SARS-associated virus.

AYUSH 64

Ayush-64 is a patented anti-malarial medicine developed by the Central Council for Research in Ayurvedic Sciences (CCRAS). It is a combination of 4 Ayurvedic drugs Saptaparna stem bark (Alstonia scholaris), Katuki roots (Picrorhiza kurroa), Chirayata whole plant (Swertia Chirata) and Kuberakshaa seed (Caesalpinia crista). National task force for COVID-19 constituted by ICMR recommends the use of Hydroxychloroquine (HCQ) for prophylaxis of SARS-CoV-2 infection for high risk population. Now plans to check the efficacy of Ayush-64 medicine for the same.

In Ayurveda, Rasayana is mentioned which can be helpful to accomplish a prolonged happy and healthy life. In concern to SARS-CoV-2 infection, Rasayan therapy may have benefits in many ways such as cutback in recovery time, reduction in duration of stay in hospital, enrichment in clinical cure rate and prevention from ailment. In the present scenario, India needs fast-track clinical trials on Ayurvedic Rasayan such as Ashwagandha (Withania somnifera), Pippali ((Piper longum), Shatavari (Asparagus racemosus), Guduchi (Tinospora cordifolia), Yashtimadhu (Glycyrrhiza Glabra) and Aamalaki (Phyllanthus emblica) for prophylaxis of SARS-CoV-2 infection.

CONCLUSION

Coronavirus disease 2019 (COVID-19) is an infection caused by the novel coronavirus severe acute respiratory coronavirus 2 (SARS-CoV-2). The infection manifests as a mild flu to severe acute respiratory infection. The World Health Organization (WHO) declared COVID-19 as a global pandemic on March 11, 2020. The disease spreads by droplet infection from person to person. Currently, the laboratory diagnosis of SARS-CoV-2 is based on nucleic acid amplification tests (NAAT) like real-time reverse transcriptase (RT-PCR). At present no approved treatment or vaccine is available in all over the world for COVID-19. India has an opportunity for a worldwide leadership by developing evidence-based and scientifically proved prophylactic strategies on the basis of Ayurveda to protect people from SARS-CoV-2 infection. On March 31, 2020, Ministry of AYUSH has released its independent advisory to public for self-care measures, divided in four steps such as General Measures, Ayurvedic Immunity Promoting Measures, Ayurvedic Procedures and prophylactic treatment during dry cough / sore throat. All recommendations of AYUSH ministry have literature and scientific publication support. It is very helpful for society and after this evidence-based and scientifically proved suggestion; Government of India has planned to conduct clinical trials on three herbal drugs (Ashwagandha, Guduchi and Mulethi) and an Ayurvedic anti-malaria medicine AYUSH-64 for their preventive properties against Covid-19 infection. Rasayan therapy may have benefits like cutback in recovery time, reduction in duration of stay in hospital, enrichment in clinical cure rate and prevention from ailment. In the present scenario, fast-track clinical trials are the need of hour on Ayurvedic Rasayan such as Ashwagandha (Withania somnifera), Pippali ((Piper longum), Shatavari (Asparagus racemosus), Guduchi (Tinospora cordifolia), Yashtimadhu (Glycyrrhiza Glabra) and Aamalaki (Phyllanthus emblica) for prophylaxis of SARS-CoV-2 infection.

Abbreviations

COVID-19 = Coronavirus Disease 19
SARS-CoV-2 = Severe acute respiratory syndrome
Coronavirus
ARDS= Acute respiratory distress syndrome
RT-PCR = Real-time reverse transcription polymerase-chain-reaction
MERS -CoV= Middle East respiratory syndrome – Corona virus
SARS -CoV= Severe acute respiratory syndrome-
Coronavirus
ICTV = International Committee on Taxonomy of Viruses
NAAT = Nucleic acid amplification tests
GGO = Ground-glass opacity
NK cells = Natural killer cells
ABHRs = Alcohol-based hand rubs
ICMR = Indian Council of Medical Research
CCRAS = Central Council for Research in Ayurvedic Sciences.
CSIR = Council of Scientific & Industrial Research.

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