Covid-19 variants

Each time a virus is copied, there's some risk the host's cell will make one or more errors in the genetic code of that virus. These are known as mutations. Each new one alters the genetic blueprint of the virus a bit. Mutant viruses are known as *variants* of the original.

Many mutations won't affect how a virus works. Some might be bad for the virus. Others might improve how well the virus can infect a cell, or help the virus evade its host's immune system. A mutation might even allow the virus to resist the effects of some therapy. Scientists refer to such new-and-improved variants as *strains*.

Keep in mind that all strains of a virus are variants. Not all variants, however, are different enough to qualify as a new strain. It must have different effects.

CDC

SARS-CoV-2 Variant Classifications and Definitions

Updated Oct. 4, 2021

Key Definitions

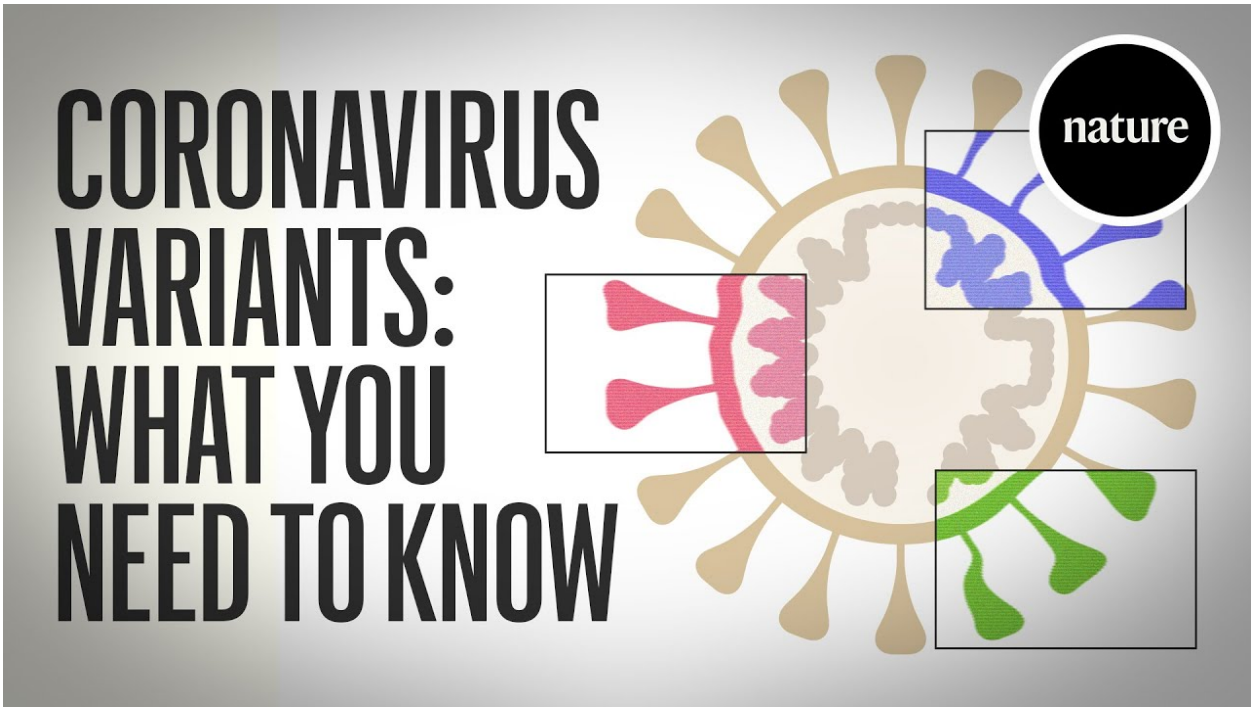
- **Mutation: A mutation refers to a single change in a virus's genome (genetic code). Mutations happen very frequently, but only sometimes change the characteristics of the virus.**
-

- **Lineage: A lineage is a group of closely related viruses with a common ancestor. SARS-CoV-2 has many lineages; all cause COVID-19.**
-
- **Variant: A variant is a viral genome (genetic code) that may contain one or more mutations. In some cases, a group of variants with similar genetic changes, such as a lineage or group of lineages, may be designated by public health organizations as a Variant of Concern or a Variant of Interest due to shared attributes and characteristics that may require public health action.**

    - Variant Being Monitored (VBM)
        - Alpha (B.1.1.7 and Q lineages)
        - Beta (B.1.351 and descendent lineages)
        - Gamma (P.1 and descendent lineages)
        - Epsilon (B.1.427 and B.1.429)
        - Eta (B.1.525)
        - Iota (B.1.526)
        - Kappa (B.1.617.1)
        - 1.617.3
        - Mu (B.1.621, B.1.621.1)
        - Zeta (P.2)
    - Variant of Interest (VOI)
    - Variant of Concern (VOC)
        - Delta (B.1.617.2 and AY lineages)
    - Variant of High Consequence (VOHC)

- To date, no variants of high consequence have been identified in the United States.

U-tube Explaining Variants of Coronavirus.



COVID-19 (coronavirus): Long-term effects byMayo Clinic

COVID-19 symptoms can sometimes persist for months. The virus can damage the lungs, heart and brain, which increases the risk of long-term health problems.

By Mayo Clinic Staff

Most people who have coronavirus disease 2019 (COVID-19) recover completely within a few weeks. But some people — even

those who had mild versions of the disease — continue to experience symptoms after their initial recovery.

These people sometimes describe themselves as "long haulers" and the conditions have been called post-COVID-19 syndrome or "long COVID-19." These health issues are sometimes called post-COVID-19 conditions. They're generally considered to be effects of COVID-19 that persist for more than four weeks after you've been diagnosed with the COVID-19 virus.

Older people and people with many serious medical conditions are the most likely to experience lingering COVID-19 symptoms, but even young, otherwise healthy people can feel unwell for weeks to months after infection. Common signs and symptoms that linger over time include:

- Fatigue
- Shortness of breath or difficulty breathing
- Cough
- Joint pain
- Chest pain
- Memory, concentration or sleep problems
- Muscle pain or headache
- Fast or pounding heartbeat
- Loss of smell or taste
- Depression or anxiety
- Fever
- Dizziness when you stand
- Worsened symptoms after physical or mental activities

Organ damage caused by COVID-19

Although COVID-19 is seen as a disease that primarily affects the lungs, it can also damage many other organs, including the heart,

kidneys and the brain. Organ damage may lead to health complications that linger after COVID-19 illness. In some people, lasting health effects may include long-term breathing problems, heart complications, chronic kidney impairment, stroke and Guillain-Barre syndrome — a condition that causes temporary paralysis.

Some adults and children experience multi-system inflammatory syndrome after they have had COVID-19. In this condition, some organs and tissues become severely inflamed.

SARS-CoV-2 and the Brain

J Exp Med

. 2021 Mar 1;218(3):e20202135. doi: 10.1084/jem.20202135.

Neuroinvasion of SARS-CoV-2 in human and mouse brain

Eric Song # 1 , Ce Zhang # 2 3 , Benjamin Israelow 1 4 , Alice Lu-Culligan 1 , Alba Vieites Prado 5 , Sophie Skriabine 5 , Peiwen Lu 1 , Orr-El Weizman 1 , Feimei Liu 1 6 , Yile Dai 1 , Klara Szigeti-Buck 7 , Yuki Yasumoto 7 , Guilin Wang 8 , Christopher Castaldi 8 , Jaime Heltke 8 , Evelyn Ng 8 , John Wheeler 8 , Mia Madel Alfajaro 1 9 , Etienne Levavasseur 5 , Benjamin Fontes 10 , Neal G Ravindra 11 12 , David Van Dijk 11 12 , Shrikant Mane 2 8 , Murat Gunel 2 3

13 , Aaron Ring 1 , Syed A Jaffar Kazmi 14 , Kai Zhang 14 , Craig B Wilen 1 9 , Tamas L Horvath 7 , Isabelle Plu 5 15 , Stephane Haik 5 10 15 16 , Jean-Leon Thomas 5 17 , Angeliki Louvi 3 13 , Shelli F Farhadian 4 17 , Anita Huttner 18 , Danielle Seilhean 5 15 , Nicolas Renier 5 , Kaya Bilguvar 2 8 , Akiko Iwasaki 1 19 20
Affiliations collapse
Affiliations

- 1
Department of Immunobiology, Yale School of Medicine, New Haven, CT.
- 2
Department of Genetics, Yale School of Medicine, New Haven, CT.
- 3
Department of Neuroscience, Yale School of Medicine, New Haven, CT.
- 4
Department of Internal Medicine, Section of Infectious Diseases, Yale School of Medicine, New Haven, CT.
- 5
Sorbonne Université, INSERM U1127, French National Centre for Scientific Research, Joint Research Unit 7225, Paris Brain Institute, Institut du Cerveau et de la Moelle Épinière, Paris, France.
- 6
Department of Biomedical Engineering, Yale University, New Haven, CT.
- 7
Department of Comparative Medicine, Yale School of Medicine, New Haven, CT.
- 8
Yale Center for Genome Analysis, West Haven, CT.

- 9
  Department of Laboratory Medicine, Yale School of Medicine, New Haven, CT.
- 10
  Yale Environmental Health and Safety, Yale University, New Haven, CT.
- 11
  Cardiovascular Research Center, Section of Cardiovascular Medicine, Department of Internal Medicine, Yale School of Medicine, New Haven, CT.
- 12
  Department of Computer Science, Yale University, New Haven, CT.
- 13
  Department of Neurosurgery, Yale School of Medicine, New Haven, CT.
- 14
  Department of Laboratory Medicine, Geisinger Medical Center, Danville, PA.
- 15
  Assistance Publique Hôpitaux de Paris, Hôpital Pitié-Salpêtrière, Département de Neuropathologie, Paris, France.
- 16
  Assistance Publique Hôpitaux de Paris, Hôpital Pitié-Salpêtrière, Cellule nationale de référence des maladies de Creutzfeldt-Jakob, Paris, France.
- 17
  Department of Neurology, Yale School of Medicine, New Haven, CT.
- 18
  Department of Pathology, Yale School of Medicine, New Haven, CT.

- [19] Department of Molecular, Cellular, and Developmental Biology, Yale School of Medicine, New Haven, CT.
- [20] Howard Hughes Medical Institute, Chevy Chase, MD.

[#] Contributed equally.

- PMID: 33433624 PMCID: PMC7808299 DOI: 10.1084/jem.20202135

Free PMC article

Abstract

Although COVID-19 is considered to be primarily a respiratory disease, SARS-CoV-2 affects multiple organ systems including the central nervous system (CNS). Yet, there is no consensus on the consequences of CNS infections. **Here, we used three independent approaches to probe the capacity of SARS-CoV-2 to infect the brain. First, using human brain organoids, we observed clear evidence of infection with accompanying metabolic changes in infected and neighboring neurons. However, no evidence for type I interferon responses was detected. We demonstrate that neuronal infection can be prevented by blocking ACE2 with antibodies or by administering cerebrospinal fluid from a COVID-19 patient. Second, using mice overexpressing human ACE2, we demonstrate SARS-CoV-2 neuroinvasion in vivo. Finally, in autopsies from patients who died of COVID-19, we detect SARS-CoV-2 in cortical neurons and note pathological features associated with infection with minimal immune cell infiltrates. These results provide evidence for the neuroinvasive capacity of SARS-CoV-2 and an unexpected consequence of direct infection of neurons by SARS-CoV-2.**

Prions

Review

Annu Rev Pathol

actions

- Search in PubMed
- Search in NLM Catalog
- Add to Search

. 2019 Jan 24;14:497-516. doi: 10.1146/annurev-pathmechdis-012418-013109. Epub 2018 Oct 24.

Cellular and Molecular Mechanisms of Prion Disease

Christina J Sigurdson 1, Jason C Bartz 2, Markus Glatzel 3

Affiliations collapse

Affiliations

- 1 Departments of Pathology and Medicine, UC San Diego School of Medicine, University of California, San Diego, La Jolla, California 92093, USA; email: csigurdson@ucsd.edu.
- 2 Department of Medical Microbiology and Immunology, Creighton University, Omaha, Nebraska 68178, USA.
- 3 Institute of Neuropathology, University Medical Center Hamburg-Eppendorf, 20246 Hamburg, Germany.

- PMID: 30355150 DOI: 10.1146/annurev-pathmechdis-012418-013109

Abstract

Prion diseases are rapidly progressive, incurable neurodegenerative disorders caused by misfolded,

aggregated proteins known as prions, which are uniquely infectious. Remarkably, these infectious proteins have been responsible for widespread disease epidemics, including kuru in humans, bovine spongiform encephalopathy in cattle, and chronic wasting disease in cervids, the latter of which has spread across North America and recently appeared in Norway and Finland. The hallmark histopathological features include widespread spongiform encephalopathy, neuronal loss, gliosis, and deposits of variably sized aggregated prion protein, ranging from small, soluble oligomers to long, thin, unbranched fibrils, depending on the disease. Here, we explore recent advances in prion disease research, from the function of the cellular prion protein to the dysfunction triggering neurotoxicity, as well as mechanisms underlying prion spread between cells. We also highlight key findings that have revealed new therapeutic targets and consider unanswered questions for future research.

Keywords: amyloid; neurodegeneration; neurotoxicity; prion transmission; strains.

Case Reports
Brain Behav Immun
actions

- Search in PubMed
- Search in NLM Catalog
- Add to Search

. 2020 Oct;89:601-603. doi: 10.1016/j.bbi.2020.07.007. Epub 2020 Jul 15.

Creutzfeldt-Jakob disease in a man with COVID-19: SARS-CoV-2-accelerated neurodegeneration?

Michael J Young 1 , Meabh O'Hare 2 , Marcelo Matiello 2 , Jeremy D Schmahmann 2
Affiliations collapse
Affiliations

- 1 Department of Neurology, Massachusetts General Hospital, Harvard Medical School, United States. Electronic address: michael.young@mgh.harvard.edu.
- 2 Department of Neurology, Massachusetts General Hospital, Harvard Medical School, United States.
- PMID: 32681865 PMCID: PMC7362815 DOI: 10.1016/j.bbi.2020.07.007

Free PMC article

Abstract

We describe a man whose first manifestations of Creutzfeldt-Jakob disease occurred in tandem with symptomatic onset of coronavirus disease 2019 (COVID-19). Drawing from recent data on prion disease pathogenesis and immune responses to SARS-CoV-2, we hypothesize that the cascade of systemic inflammatory mediators in response to the virus accelerated the pathogenesis of our patient's prion disease. This hypothesis introduces the potential relationship between immune responses to the novel coronavirus and the hastening of preclinical or manifest neurodegenerative disorders. The global prevalence of both COVID-19 and neurodegenerative disorders adds urgency to the study of this potential relationship.

Keywords: COVID-19; Neurodegeneration; Prion disease; Psychoneuroimmunology.

Review
Pathogens
actions
- Search in PubMed
- Search in NLM Catalog
- Add to Search
. 2020 Mar 14;9(3):216. doi: 10.3390/pathogens9030216.

Immunotherapy against Prion Disease

Yue Ma 1 , Jiyan Ma 1
Affiliations collapse
Affiliation

- 1
  Center for Neurodegenerative Science, Van Andel Institute, 333 Bostwick Avenue N.E., Grand Rapids, MI 49503, USA.
- PMID: 32183309 PMCID: PMC7157205 DOI: 10.3390/pathogens9030216

Free PMC article

Abstract

The term "prion disease" encompasses a group of neurodegenerative diseases affecting both humans and animals. Currently, there is no effective therapy and all forms of prion disease are invariably fatal. Because of (a) the outbreak of bovine spongiform encephalopathy in cattle and variant Creutzfeldt-Jakob disease in humans; (b) the heated debate about the prion hypothesis; and (c) the availability of a natural prion disease in rodents, the understanding of the pathogenic process in prion disease is much more advanced compared to that of other neurodegenerative disorders, which inspired many attempts to develop therapeutic strategies against these fatal diseases. In this review, we

focus on immunotherapy against prion disease. We explain our rationale for immunotherapy as a plausible therapeutic choice, review previous trials using either active or passive immunization, and discuss potential strategies for overcoming the hurdles in developing a successful immunotherapy. We propose that immunotherapy is a plausible and practical therapeutic strategy and advocate more studies in this area to develop effective measures to control and treat these devastating disorders.

Handb Clin Neurol

. 2018;153:419-430. doi: 10.1016/B978-0-444-63945-5.00023-4.

Vaccination strategies

Thomas Wisniewski [1], Fernando Goñi [2]
Affiliations collapse
Affiliations
- 1
Center for Cognitive Neurology, New York University School of Medicine, New York, NY, United States; Department of Neurology, New York University School of Medicine, New York, NY, United States; Department of Pathology, New York University School of Medicine, New York, NY, United States; Department of Psychiatry, New York University School of Medicine, New York, NY, United States. Electronic address: thomas.wisniewski@nyumc.org.
- 2
Center for Cognitive Neurology, New York University School

of Medicine, New York, NY, United States; Department of Neurology, New York University School of Medicine, New York, NY, United States.
- PMID: 29887149 DOI: 10.1016/B978-0-444-63945-5.00023-4

Abstract

Currently all prion diseases are without effective treatment and are universally fatal. It is increasingly being recognized that the pathogenesis of many neurodegenerative diseases, such as Alzheimer disease (AD), includes "prion-like" properties. Hence, any effective therapeutic intervention for prion disease could have significant implications for other neurodegenerative diseases. Conversely, therapies that are effective in AD might also be therapeutically beneficial for prion disease. AD-like prion disease has no effective therapy. **However, various vaccine and immunomodulatory approaches have shown great success in animal models of AD, with numerous ongoing clinical trials of these potential immunotherapies. More limited evidence suggests that immunotherapies may be effective in prion models and in naturally occurring prion disease. In particular, experimental data suggest that mucosal vaccination against prions can be effective for protection against orally acquired prion infection. Many prion diseases, including natural sheep scrapie, bovine spongiform encephalopathy, chronic wasting disease, and variant Creutzfeldt-Jakob disease, are thought to be acquired peripherally, mainly by oral exposure. Mucosal vaccination would be most applicable to this form of transmission. In this chapter we review various immunologically based strategies which are under development for prion infection.**

Keywords: Creutzfeldt–Jakob disease; bovine spongiform encephalopathy; chronic wasting disease; immunomodulation; mucosal immunization; prion disease; vaccine.

Review

Acta Biochim Biophys Sin (Shanghai)

. 2013 Jun;45(6):494-502. doi: 10.1093/abbs/gmt022. Epub 2013 Mar 3.

Role of autophagy in prion protein-induced neurodegenerative diseases

Hao Yao 1, Deming Zhao, Sher Hayat Khan, Lifeng Yang

Affiliations expand

- PMID: 23459558 DOI: 10.1093/abbs/gmt022

Abstract

Prion diseases, characterized by spongiform degeneration and the accumulation of misfolded and aggregated PrP(Sc) in the central nervous system, are one of fatal neurodegenerative and infectious disorders of humans and animals. In earlier studies, autophagy vacuoles in neurons were frequently observed in neurodegenerative diseases such as Alzheimer's, Parkinson's, and Huntington's diseases as well as prion diseases. Autophagy is a highly conserved homeostatic process by which several cytoplasmic components (proteins or organelles) are sequestered in a

double-membrane-bound vesicle termed 'autophagosome' and degraded upon their fusion with lysosome. The pathway of intercellular self-digestion at basal physiological levels is indispensable for maintaining the healthy status of tissues and organs. In case of prion infection, increasing evidence indicates that autophagy has a crucial ability of eliminating pathological PrP(Sc) accumulated within neurons. In contrast, autophagy dysfunction in affected neurons may contribute to the formation of spongiform changes. In this review, we summarized recent findings about the effect of mammalian autophagy in neurodegenerative disorders, particularly in prion diseases. We also summarized the therapeutic potential of some small molecules (such as lithium, rapamycin, Sirtuin 1 and resveratrol) targets to mitigate such diseases on brain function. Furthermore, we discussed the controversial role of autophagy, whether it mediates neuronal toxicity or serves a protective function in neurodegenerative disorders.

Keywords: autophagy; neurodegenerative disease; prion protein.

Neuroprotection and Phytosterol

92 PubMed articles
29Nov2021

- Review

Biomedicines

actions

- Search in PubMed
- Search in NLM Catalog
- Add to Search

. 2020 Aug 12;8(8):284. doi: 10.3390/biomedicines8080284.

Neuroprotection: Targeting Multiple Pathways by Naturally Occurring Phytochemicals

Andleeb Khan 1, Sadaf Jahan 2, Zuha Imtiyaz 3, Saeed Alshahrani 1, Hafiz Antar Makeen 4, Bader Mohammed Alshehri 2, Ajay Kumar 5, Azher Arafah 6, Muneeb U Rehman 6
Affiliations expand

- PMID: 32806490 PMCID: PMC7459826 DOI: 10.3390/biomedicines8080284

Free PMC article

Abstract

With the increase in the expectancy of the life span of humans, neurodegenerative diseases (NDs) have imposed a considerable burden on the family, society, and nation. In defiance of the breakthroughs in the knowledge of the pathogenesis and underlying mechanisms of various NDs, very little success has been achieved in developing effective therapies. This review draws a bead on the availability of the nutraceuticals to date for various NDs (Alzheimer's disease, Parkinson's disease, Amyotrophic lateral sclerosis, Huntington's disease, vascular cognitive impairment, Prion disease, Spinocerebellar ataxia, Spinal muscular atrophy, Frontotemporal dementia, and Pick's disease) focusing on their various mechanisms of action in various in vivo and in vitro models of NDs. This review is distinctive in its compilation to critically review preclinical and clinical studies of the maximum phytochemicals in amelioration and prevention of almost all kinds of neurodegenerative diseases and address their possible mechanism of action. PubMed, Embase, and Cochrane Library searches were used for preclinical studies, while ClinicalTrials.gov and PubMed were searched for clinical updates. **The results from preclinical studies**

demonstrate the efficacious effects of the phytochemicals in various NDs while clinical reports showing mixed results with promise for phytochemical use as an adjunct to the conventional treatment in various NDs. These studies together suggest that phytochemicals can significantly act upon different mechanisms of disease such as oxidative stress, inflammation, apoptotic pathways, and gene regulation. However, further clinical studies are needed that should include the appropriate biomarkers of NDs and the effect of phytochemicals on them as well as targeting the appropriate population.

Keywords: natural products; neurodegenerative diseases; neuroprotection; phytochemicals.

Review
J Diet Suppl
actions
- Search in PubMed
- Search in NLM Catalog
- Add to Search
. 2021;18(2):183-226. doi: 10.1080/19390211.2020.1741484. Epub 2020 Apr 3.

Pharmacological evaluation of Ashwagandha highlighting its healthcare claims, safety, and toxicity aspects

Deepa S Mandlik Ingawale 1 , Ajay G Namdeo 1
Affiliations expand

- PMID: 32242751 DOI: 10.1080/19390211.2020.1741484

Abstract

***Withania somnifera*, commonly known as "Ashwagandha" or "Indian ginseng" is an essential therapeutic plant of Indian subcontinent regions. It is regularly used, alone or in combination with other plants for the treatment of various illnesses in Indian Systems of Medicine over the period of 3,000 years.** Ashwagandha (*W. somnifera*) belongs to the genus *Withania* and family *Solanaceae.* It comprises a broad spectrum of phytochemicals having wide range of biological effects. ***W. somnifera* has demonstrated various biological actions such as anti-cancer, anti-inflammatory, anti-diabetic, anti-microbial, anti-arthritic, anti-stress/adaptogenic, neuro-protective, cardio-protective, hepato-protective, immunomodulatory properties. Furthermore, *W. somnifera* has revealed the capability to decrease reactive oxygen species and inflammation, modulation of mitochondrial function, apoptosis regulation and improve endothelial function. Withaferin-A is an important phytoconstituents of *W. somnifera* belonging to the category of withanolides been used in the traditional system of medicine for the treatment of various disorders. In this review, we have summarized the active phytoconstituents, pharmacologic activities (preclinical and clinical), mechanisms of action, potential beneficial applications, marketed formulations and safety and toxicity profile of *W. somnifera*.**

Keywords: Withania somnifera; adaptogenic; anti-Alzheimer; anti-Parkinson; anti-arthritic; anti-cancer; anti-diabetic; anti-hypoxic; anti-inflammatory; anti-ischemic; anti-microbial; anti-stress; aphrodisiac; cardio-protective; clinical evaluation; hepatoprotection; immunomodulatory; neuro-protective; safety and toxicity.

Hydroxychloroquine and COVID-19

3,155 Pubmed Articles
29November2021

Int J Antimicrob Agents
actions

- Search in PubMed
- Search in NLM Catalog
- Add to Search

. 2020 Jul;56(1):105949. doi: 10.1016/j.ijantimicag.2020.105949. Epub 2020 Mar 20.

Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial

Philippe Gautret [1], Jean-Christophe Lagier [2], Philippe Parola [1], Van Thuan Hoang [3], Line Meddeb [4], Morgane Mailhe [4], Barbara Doudier [4], Johan Courjon [5], Valérie Giordanengo [6], Vera Esteves Vieira [4], Hervé Tissot Dupont [2], Stéphane Honoré [7], Philippe Colson [2], Eric Chabrière [2], Bernard La Scola [2], Jean-Marc Rolain [2], Philippe Brouqui [2], Didier Raoult [8]
Affiliations collapse

Affiliations

- [1] IHU-Méditerranée Infection, Marseille, France; Aix Marseille Univ, IRD, AP-HM, SSA, VITROME, Marseille, France.
- [2] IHU-Méditerranée Infection, Marseille, France; Aix Marseille Univ, IRD, APHM, MEPHI, Marseille, France.

- 3 IHU-Méditerranée Infection, Marseille, France; Aix Marseille Univ, IRD, AP-HM, SSA, VITROME, Marseille, France; Thai Binh University of Medicine and Pharmacy, Thai Binh, Viet Nam.
- 4 IHU-Méditerranée Infection, Marseille, France.
- 5 Infectiologie, Hôpital de l'Archet, Centre Hospitalier Universitaire de Nice, Nice, France; Université Côte d'Azur, Nice, France; U1065, Centre Méditerranéen de Médecine Moléculaire, C3M, Virulence Microbienne et Signalisation Inflammatoire, INSERM, Nice, France.
- 6 Department of Virology, Biological and Pathological Center, Centre Hospitalier Universitaire de Nice, 06200 Nice, France.
- 7 Service Pharmacie, Hôpital Timone, AP-HM, Marseille, France; Laboratoire de Pharmacie Clinique, Aix Marseille Université, Marseille, France.
- 8 IHU-Méditerranée Infection, Marseille, France; Aix Marseille Univ, IRD, APHM, MEPHI, Marseille, France. Electronic address: Didier.raoult@gmail.com.

- PMID: 32205204 PMCID: PMC7102549 DOI: 10.1016/j.ijantimicag.2020.105949

Free PMC article

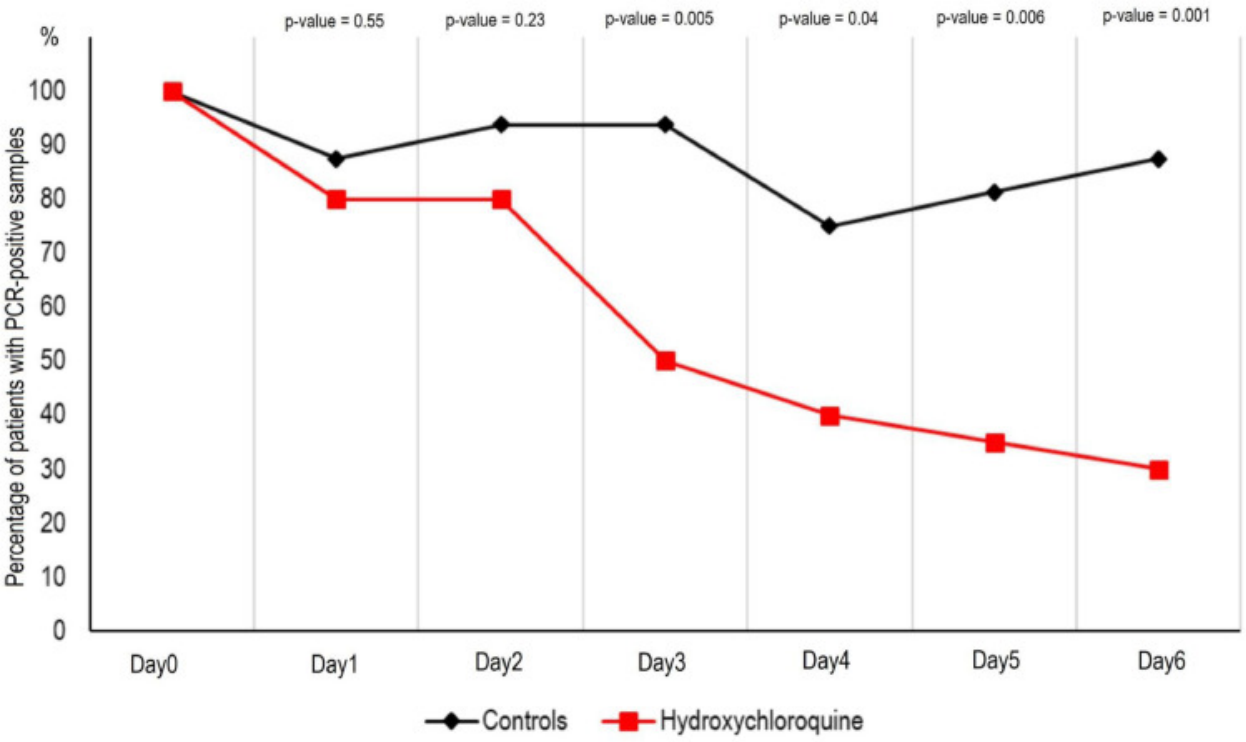
Abstract

Background: Chloroquine and hydroxychloroquine have been found to be efficient on SARS-CoV-2, and reported to be efficient in Chinese COV-19 patients. We evaluate the effect of hydroxychloroquine on respiratory viral loads.

Patients and methods: French Confirmed COVID-19 patients were included in a single arm protocol from early March to March

16th, to receive 600mg of hydroxychloroquine daily and their viral load in nasopharyngeal swabs was tested daily in a hospital setting. Depending on their clinical presentation, azithromycin was added to the treatment. Untreated patients from another center and cases refusing the protocol were included as negative controls. Presence and absence of virus at Day6-post inclusion was considered the end point.

Results: Six patients were asymptomatic, 22 had upper respiratory tract infection symptoms and eight had lower respiratory tract infection symptoms. Twenty cases were treated in this study and showed a significant reduction of the viral carriage at D6-post inclusion compared to controls, and much lower average carrying duration than reported in the litterature for



untreated patients. Azithromycin added to hydroxychloroquine was significantly more efficient for virus elimination.

Conclusion: Despite its small sample size, our survey shows that hydroxychloroquine treatment is significantly associated with viral

load reduction/disappearance in COVID-19 patients and its effect is reinforced by azithromycin.

Keywords: 2019-nCoV; Azithromycin; COVID-19; Clinical trial; Hydroxychloroquine; SARS-CoV-2.

Review
New Microbes New Infect
actions

- Search in PubMed
- Search in NLM Catalog
- Add to Search

. 2020 Apr 22;35:100684. doi: 10.1016/j.nmni.2020.100684. eCollection 2020 May.

Potential use of hydroxychloroquine, ivermectin and azithromycin drugs in fighting COVID-19: trends, scope and relevance

R Choudhary [1], A K Sharma [1]
Affiliations expand

- PMID: 32322397 PMCID: PMC7175902 DOI: 10.1016/j.nmni.2020.100684

Free PMC article

Abstract

Alarming situation has been caused due to the emergence of COVID-19 infection around the world. There is an urgency of developing a therapeutic strategy in order to control the spread of COVID-19. **Towards that initiative, potential drugs like**

hydroxychloroquine, ivermectin and azithromycin have been tested by diverse group of researchers worldwide for their potential against novel coronavirus. The present report presents together the comprehensive knowledge derived from the major researches about the above drugs altogether in context of the current health emergency around the world. Hydroxychloroquine and ivermectin were known to act by creating the acidic environment and inhibiting the importin (IMPα/β1) mediated viral import. Azithromycin was found to act similar to the hydroxychloroquine as an acidotropic lipophilic weak base. All the three categories of drugs seemed to potentially act against novel coronavirus infection. However, their efficacies need to be studied in detail individually and in combination in-vivo in order to combat COVID-19 infection.

Keywords: Azithromycin; COVID-19; coronavirus; hydroxychloroquine; ivermectin.

Ivermectin and Covid-19

Review
Pharmacol Rep

. 2021 Jun;73(3):736-749. doi: 10.1007/s43440-020-00195-y. Epub 2021 Jan 3.

Ivermectin as a potential drug for treatment of COVID-19: an in-sync review with clinical and computational attributes

Harpinder Kaur [1], Nishant Shekhar [1], Saurabh Sharma [1], Phulen Sarma [1], Ajay Prakash [1], Bikash Medhi [2]
Affiliations collapse

Affiliations

- [1] Department of Pharmacology, Post Graduate Institute of Medical Education and Reseasrch (PGIMER), Chandigarh, 160012, India.
- [2] Department of Pharmacology, Post Graduate Institute of Medical Education and Reseasrch (PGIMER), Chandigarh, 160012, India. drbikashus@yahoo.com.
- PMID: 33389725 PMCID: PMC7778723 DOI: 10.1007/s43440-020-00195-y

Free PMC article

Abstract

Introduction: COVID-19 cases are on surge; however, there is no efficient treatment or vaccine that can be used for its management. Numerous clinical trials are being reviewed for use of different drugs, biologics, and vaccines in COVID-19. A much empirical approach will be to repurpose existing drugs for which pharmacokinetic and safety data are available, because this will facilitate the process of drug development. The article discusses the evidence available for the use of Ivermectin, an anti-parasitic drug with antiviral properties, in COVID-19.

Methods: A rational review of the drugs was carried out utilizing their clinically significant attributes. A more thorough understanding was met by virtual embodiment of the drug

structure and realizable viral targets using artificial intelligence (AI)-based and molecular dynamics (MD)-simulation-based study.

Conclusion: Certain studies have highlighted the significance of ivermectin in COVID-19; however, it requires evidences from more Randomised Controlled Trials (RCTs) and dose- response studies to support its use. In silico-based analysis of ivermectin's molecular interaction specificity using AI and classical mechanics simulation-based methods indicates positive interaction of ivermectin with viral protein targets, which is leading for SARS-CoV 2 N-protein NTD (nucleocapsid protein N-terminal domain).

Keywords: COVID-19; Ivermectin; SARS-CoV-2; Treatment.

Adaptogens and Covid-19

Nrf2 Activator and Covid-19

Both Adaptogens and Polyphenols can activate the Nrf2 pathway, For example, Amla (Emblica *officinalis*)is an adaptogen that activates the Nrf2 pathway, (See what it can do below). It removes cellular trash, (misfolded proteins, both organic xenobiotics ie. parts of viruses and toxic metals. It fixes or restores you energy producing mitochondria and restore life to cells by activating telomerase. It makes you fell young again.

Antiviral
Review
Pharmaceuticals (Basel)
actions:
. 2020 Sep 8;13(9):236. doi: 10.3390/ph13090236.

The Role of Adaptogens in Prophylaxis and Treatment of Viral Respiratory Infections

Alexander Panossian 1 2 , Thomas Brendler 3 4 5
Affiliations collapse
Affiliations
- 1
Phytomed AB, Vaxtorp, 31275 Halland, Sweden.
- 2
EuropharmaUSA, Green Bay, WI 54311, USA.
- 3
Department of Botany and Plant Biotechnology, University of Johannesburg, Johannesburg 2000, South Africa.
- 4
Traditional Medicinals Inc., Rohnert Park, CA 94928, USA.
- 5
Plantaphile, Collingswood, NJ 08108, USA.
- PMID: 32911682 PMCID: PMC7558817 DOI: 10.3390/ph13090236

Abstract
The aim of our review is to demonstrate the potential of herbal preparations, specifically adaptogens for prevention and treatment of respiratory infections, as well as convalescence, specifically through supporting a challenged immune system, increasing resistance to viral infection, inhibiting severe inflammatory progression, and driving effective recovery. The evidence from pre-clinical and clinical studies with *Andrographis paniculata*, *Eleutherococcus senticosus*, *Glycyrrhiza* spp., *Panax* spp., *Rhodiola rosea*, *Schisandra chinensis*, ***Withania somnifera***, their combination products and melatonin suggests that **adaptogens can be useful in prophylaxis and treatment of viral infections at all stages of progression of inflammation as well as in aiding recovery of the organism by (i) modulating innate and adaptive immunity, (ii) anti-inflammatory activity, (iii) detoxification and repair of oxidative stress-induced damage in compromised cells, (iv) direct antiviral effects of inhibiting viral docking or replication, and (v) improving quality of life during convalescence.**
Keywords: Andrographis; Eleutherococcus; Glycyrrhiza; Panax; Rhodiola; Schisandra; Withania; adaptogens; melatonin; viral infection.
Conflict of interest statement
The authors declare no conflict of interest.

Sheng Li Xue Bao
actions:
. 2015 Feb 25;67(1):1-18.

Emblica officinalis, a master regulator of detoxification and also antioxidant, anti-inflammatory and other cytoprotective mechanisms, is raised by health promoting factors

Martin L Pall [1], Stephen Levine [2]

Affiliations

- [1] Washington State University, Portland, Oregon 97232-3312, USA. martin_pall@wsu.edu.
- [2] Allergy Research Group, Alameda, California 94502, USA.

- PMID: 25672622

Free article

Abstract

The transcription factor Nrf2, nuclear factor erythroid-2-related factor 2, activates the transcription of over 500 genes in the human genome, most of which have cytoprotective functions. Nrf2 produces cytoprotection by detoxification mechanisms leading to increased detoxification and excretion of both organic xenobiotics and toxic metals; its action via over two dozen genes increases highly coordinated antioxidant activities; it produces major anti-inflammatory changes; it stimulates mitochondrial biogenesis and otherwise improves mitochondrial function; and it stimulates autophagy, removing toxic protein aggregates and dysfunctional organelles. Health-promoting nutrients and other factors act, at least in part by raising Nrf2 including: many phenolic antioxidants; gamma- and delta-tocopherols and tocotrienols; long chain omega-3 fatty acids DHA and EPA; many carotenoids of which lycopene may be the most active; isothiocyanates from cruciferous vegetables; sulfur compounds from allium vegetables; terpenoids. Other health promoting, Nrf2 raising factors include low level oxidative stress (hormesis), exercise and caloric restriction. **Raising Nrf2 has been found to prevent and/or**

treat a large number of chronic inflammatory diseases in animal models and/or humans including various cardiovascular diseases, kidney diseases, lung diseases, diseases of toxic liver damage, cancer (prevention), diabetes/metabolic syndrome/obesity, sepsis, autoimmune diseases, inflammatory bowel disease, HIV/AIDS and epilepsy. Lesser evidence suggests that raising Nrf2 may lower 16 other diseases. Many of these diseases are probable NO/ONOO(-) cycle diseases and Nrf2 lowers effects of NO/ONOO(-) cycle elements. **The most healthful diets known, traditional Mediterranean and Okinawan, are rich in Nrf2 raising nutrients as apparently was the Paleolithic diet that our ancestors ate. Modern diets are deficient in such nutrients. Nrf2 is argued to be both lifespan and health-span extending. Possible downsides to too much Nrf2 are also discussed. Nrf2 is not a magic bullet but is likely to be of great importance in health promotion, particularly in those regularly exposed to toxic chemicals.**