

## NATURE REVIEWS IMMUNOLOGY

Check for updates

## COVID-19: the vasculature unleashed

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On the basis of emerging evidence from patients with COVID-19, we postulate that endothelial cells are essential contributors to the initiation and propagation of severe COVID-19. Here, we discuss current insights into the link between endothelial cells, viral infection and inflammatory changes and propose novel therapeutic strategies.

Journal of  
Clinical Medicine

MDPI

Review

## Hypertension, Thrombosis, Kidney Failure, and Diabetes: Is COVID-19 an Endothelial Disease? A Comprehensive Evaluation of Clinical and Basic Evidence

## Endothelial cell infection and endotheliitis in COVID-19

www.thelancet.com Vol 395 May 2, 2020

## In the news

COVID-19 Autopsies Put Endothelial Damage, Angiogenesis in the Spotlight | tctmd.com

6/15/20, 9:16 AM

tctMD/the heart beat

NEWS

## COVID-19 Autopsies Put Endothelial Damage, Angiogenesis in the Spotlight

Microbes and Infection 22 (2020) 149–150

Contents lists available at ScienceDirect

Microbes and Infection

journal homepage: [www.elsevier.com/locate/micinf](http://www.elsevier.com/locate/micinf)

Letter to the editor

Covid-19 accelerates endothelial dysfunction and nitric oxide deficiency

ESC  
European Society  
of CardiologyCardiovascular Research (2020)  
doi:10.1093/cvr/cvaa140

ONLINE COMMENTARIES

CARDIOVASCULAR  
RESEARCH  
OnLife

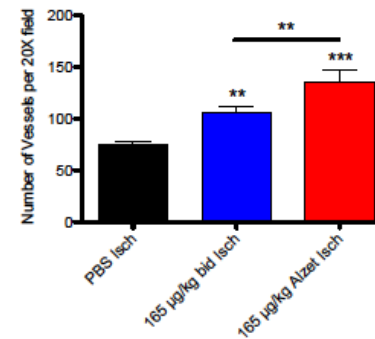
## COVID-19 as a cardiovascular disease: the potential role of chronic endothelial dysfunction

Nasdaq:JAN

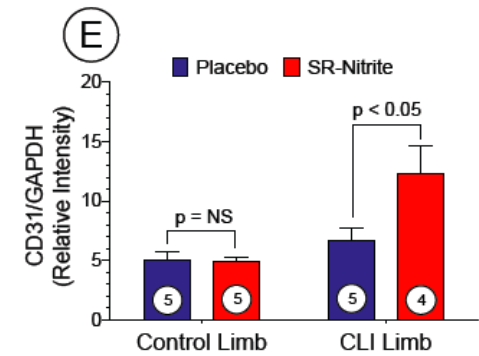
# JAN101 improves endothelial cell/vascular function

**COVID-19 is believed to attack endothelial cells** causing significant tissue inflammation and damage

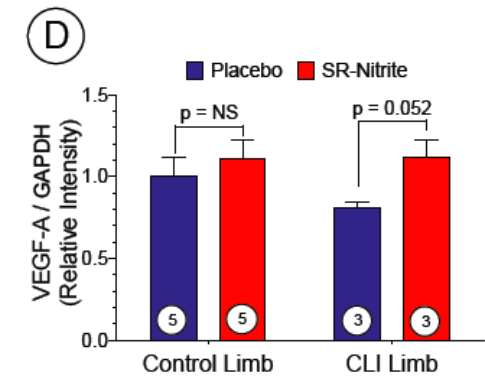
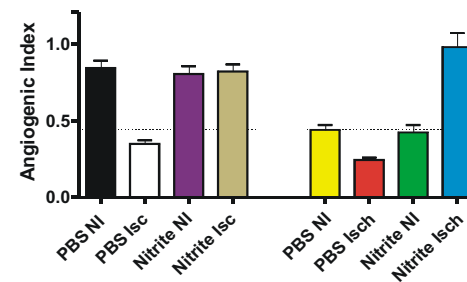
Sustained release nitrite increases vascular growth



Treatment **increases** markers for vessel growth (angiogenesis)



Nitrite therapy **induces** angiogenesis in diabetic tissue

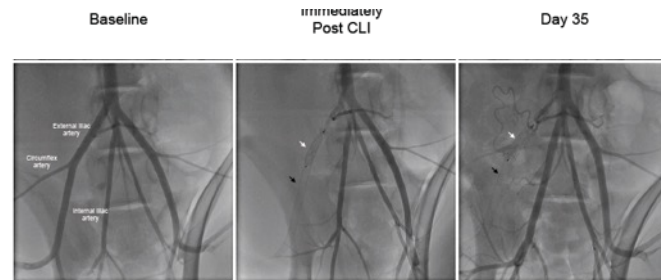


# Potential benefits of treating COVID-19 patients with sodium nitrite

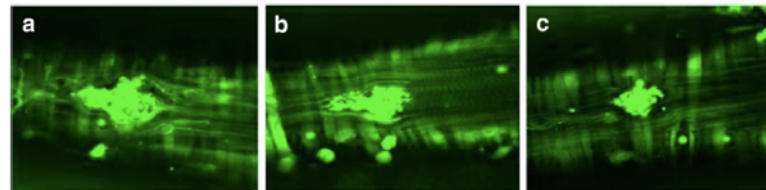
In various animal studies, JAN101 has demonstrated **positive benefits that align with COVID-19 complications**

- Reduces kidney damage
- Prevents tissue necrosis
- Reduces thrombosis
- Increases angiogenesis

## Increased angiogenesis in pigs

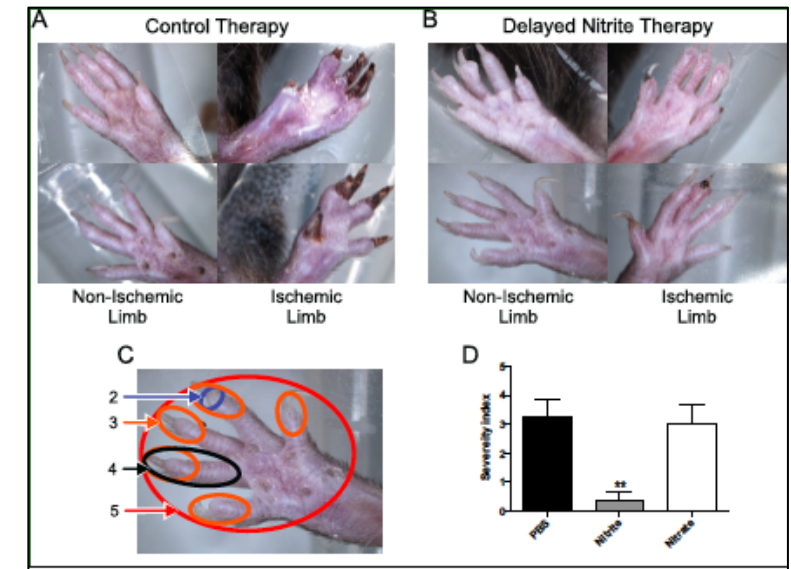


## Nitrite reduces thrombosis in mice



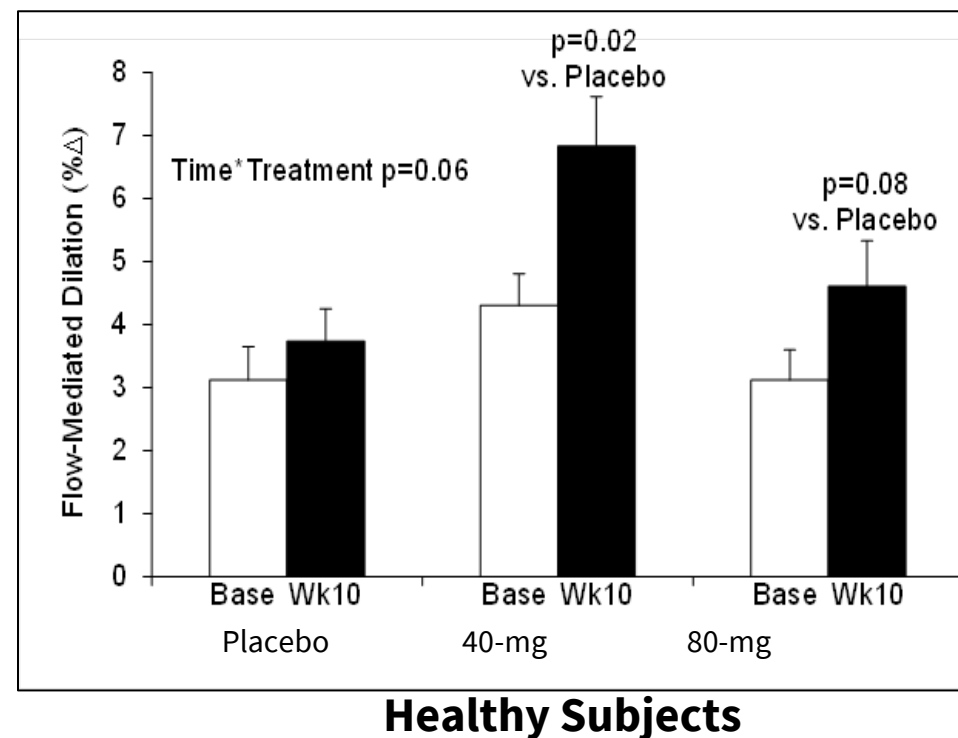
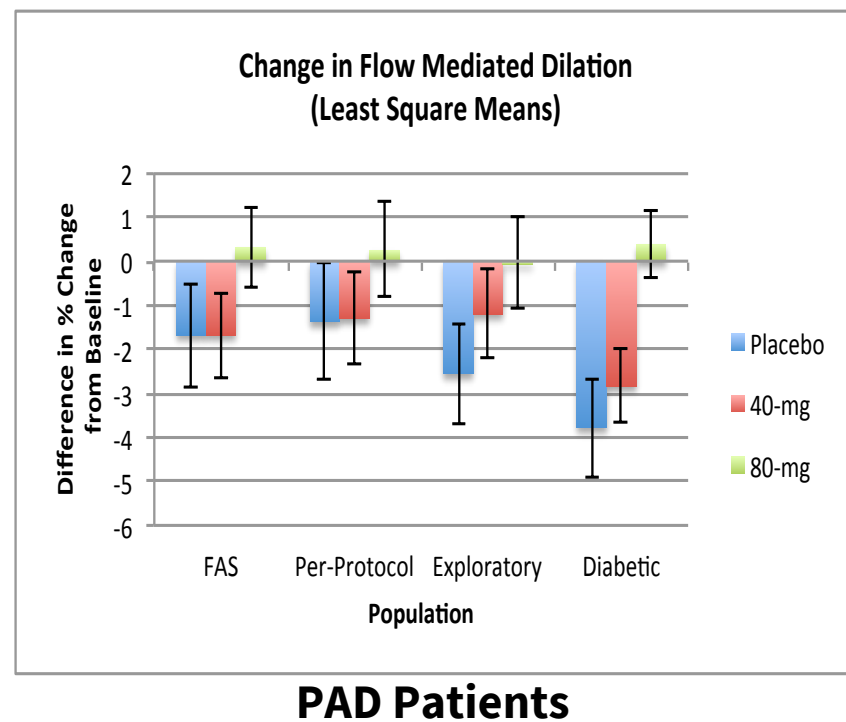
From Kramkowski et al (2017)  
Naunyn-Schmiedeberg's Arch Pharmacol 390:85-94

## Prevents tissue necrosis in diabetic mice



# Nitrite improves vascular function in humans

Using flow-mediated dilation imaging technology we can assess vascular function improvement in patients with complications including blood flow and thrombosis



# The JAN101 COVID-19 vascular treatment opportunity

As indicated in multiple human trials, our current sodium nitrate compound may be a successful treatment for the vascular complications experienced by COVID-19 patients

- Shown to improve vascular function
- Shown to reduce vascular complications such as thrombosis
- Protects major organs from tissue damage due to poor blood flow
- Inhibits inflammation, including mitigating the “cytokine storm”, a massive release of cytokine proteins that destroy endothelial cells (cells that protect the lining of vessel tissue)
- Nitrite has proven to be well tolerated and safe

## **Intend to seek emergency use authorization**

Expanding existing JAN101 IND for clinical study to treat COVID-19 vascular complications