

# Acriflavine, a clinically approved drug, inhibits SARS-CoV-2 and other betacoronaviruses

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## What is the Manuscript Microscope Sentence Audit?

The Manuscript Microscope Sentence Audit is a research paper introspection system that parses the text of your manuscript into minimal sentence components for faster, more accurate, enhanced proofreading.

## Why use a Sentence Audit to proofread your manuscript?

- **Accelerated Proofreading:** Examine long technical texts in a fraction of the usual time.
- **Superior Proofreading:** Detect subtle errors that are invisible to traditional methods.
- **Focused Proofreading:** Inspect each individual sentence component in isolation.
- **Reliable Proofreading:** Ensure every single word of your manuscript is correct.
- **Easier Proofreading:** Take the hardship out of crafting academic papers.

Bonus 1: **Improved Productivity:** Rapidly refine rough drafts to polished papers.

Bonus 2: **Improved Authorship:** Cultivate a clear, concise, consistent, writing style.

Bonus 3: **Improved Reputation:** Become known for rigorously precise publications.

**Manuscript Source:** <https://www.biorxiv.org/content/10.1101/2021.03.20.436259v1>

**Manuscript Authors:** Valeria Napolitano, Agnieszka Dabrowska, Kenji Schorpp, André Mourão, Emilia Barreto-Duran, Malgorzata Benedyk, Pawel Botwina, Stefanie Brandner, Mark Bostock, Yuliya Chykunova, Anna Czarna, Grzegorz Dubin, Tony Fröhlich, Michael Hoelscher, Malwina Jedrysik, Alex Matsuda, Katarzyna Owczarek, Magdalena Pachota, Oliver Plettenburg, Jan Potempa, Ina Rothenaigner, Florian Schlauderer, Artur Szczepanski, Kristin Greve-Isdahl Mohn, Bjorn Blomberg, Michael Sattler, Kamyar Hadian, Grzegorz Maria Popowicz & Krzysztof Pyrc

### Features of the Sentence Audit:

The Sentence Audit combines two complementary proofreading approaches:

1. Each sentence of your text is parsed and displayed in isolation for focused inspection.
2. Each individual sentence is further parsed into Minimal Sentence Components for a deeper review of the clarity, composition and consistency of the language you used.

The Minimal Sentence Components shown are the smallest coherent elements of each sentence of your text as derived from it's conjunctions, prepositions and selected punctuation symbols (i.e. commas, semicolons, round and square brackets).

The combined approaches ensure easier, faster, more effective proofreading.

### Comments and Caveats:

- The sentence parsing is achieved using a prototype natural language processing pipeline written in Python and may include occasional errors in sentence segmentation.
- Depending on the source of the input text, the Sentence Audit may contain occasional html artefacts that are parsed as sentences (E.g. "Download figure. Open in new tab").
- Always consult the original research paper as the true reference source for the text.

### Contact Information:

To get a Manuscript Microscope Sentence Audit of any other research paper, simply forward any copy of the text to [John.James@OxfordResearchServices.com](mailto:John.James@OxfordResearchServices.com).

All queries, feedback or suggestions are also very welcome.

### Research Paper Sections:

The sections of the research paper input text parsed in this audit.

[illegible]

**Title**      **Acriflavine, a clinically aproved drug, inhibits SARS-CoV-2 and other betacoronaviruses**

### **S1 [001]      Summary**

**S1 [002]**      The COVID-19 pandemic caused by SARS-CoV-2 has been socially and economically devastating.

The COVID-19 pandemic caused ...  
... by SARS-CoV-2 has been socially ...  
... and economically devastating.

**S1 [003]**      Despite an unprecedented research effort, effective therapeutics are still missing to limit severe disease and mortality.

Despite an unprecedented research effort, ...  
... effective therapeutics are still missing ...  
... to limit severe disease ...  
... and mortality.

**S1 [004]**      Using high-throughput screening, we identified acriflavine as a potent papain-like protease (PLpro) inhibitor.

Using high-throughput screening, ...  
... we identified acriflavine ...  
... as a potent papain-like protease ...  
... (PLpro) ...  
... inhibitor.

**S1 [005]**      NMR titrations and a co-crystal structure confirm that acriflavine blocks the PLpro catalytic pocket in an unexpected binding mode.

NMR titrations ...  
... and a co-crystal structure confirm ...  
... that acriflavine blocks the PLpro catalytic pocket ...  
... in an unexpected binding mode.

**S1 [006]**      We show that the drug inhibits viral replication at nanomolar concentration in cellular models, in vivo in mice and ex vivo in human airway epithelia, with broad range activity against SARS-CoV-2 and other betacoronaviruses.

We show ...  
... that the drug inhibits viral replication ...  
... at nanomolar concentration ...  
... in cellular models, ...  
... in vivo ...  
... in mice ...  
... and ex vivo ...  
... in human airway epithelia, ...

... with broad range activity ...  
... against SARS-CoV-2 ...  
... and other betacoronaviruses.

**S1 [007]** Considering that acriflavine is an inexpensive drug approved in some countries, it may be immediately tested in clinical trials and play an important role during the current pandemic and future outbreaks.

Considering ...  
... that acriflavine is an inexpensive drug approved ...  
... in some countries, ...  
... it ...  
... may be immediately tested ...  
... in clinical trials ...  
... and play an important role ...  
... during the current pandemic ...  
... and future outbreaks.

## **S2 [008] Introduction**

**S2 [009]** Coronaviruses have been considered a potential threat since 2002, when the severe, acute respiratory syndrome coronavirus (SARS-CoV) emerged in southern China spreading across continents but disappearing shortly thereafter (Drosten et al., 2003; Ksiazek et al., 2003).

Coronaviruses have been considered a potential threat ...  
... since 2002, ...  
... when the severe, ...  
... acute respiratory syndrome coronavirus ...  
... (SARS-CoV) ...  
... emerged ...  
... in southern China spreading ...  
... across continents ...  
... but disappearing shortly thereafter ...  
... (Drosten et al., 2003; ...  
... Ksiazek et al., 2003).

**S2 [010]** Ten years later, Middle-East respiratory syndrome coronavirus (MERS-CoV) posed a pandemic threat, but despite high fatality rates, the human-to-human transmission remained limited (Zaki et al., 2012).

Ten years later, ...  
... Middle-East respiratory syndrome coronavirus ...  
... (MERS-CoV) ...  
... posed a pandemic threat, ...  
... but ...  
... despite high fatality rates, ...  
... the human-to-human transmission remained limited ...  
... (Zaki et al., 2012).

**S2 [011]** Despite these warnings, the emergence of the SARS-CoV-2 and subsequent pandemic found healthcare largely unprepared and has paralyzed the modern world in an unprecedented way (Iacobucci, 2020; Ma et al., 2020; Mirzaei et al., 2020).

Despite these warnings, ...  
... the emergence ...  
... of the SARS-CoV-2 ...  
... and subsequent pandemic found healthcare largely unprepared ...  
... and has paralyzed the modern world ...  
... in an unprecedented way ...  
... (Iacobucci, 2020; ...  
... Ma et al., 2020; ...  
... Mirzaei et al., 2020).

**S2 [012]** First vaccines are available and applied already, and further approvals are expected shortly (Parker et al., 2020).

First vaccines are available ...  
... and applied already, ...  
... and further approvals are expected shortly ...  
... (Parker et al., 2020).

**S2 [013]** However, the time needed for vaccination of the global population, limited availability of vaccines, reluctance to vaccinate, and reduced effectiveness of vaccination against newly emerging variants underline the urgent need for effective antivirals (Saha et al., 2020).

However, ...  
... the time needed ...  
... for vaccination ...  
... of the global population, ...  
... limited availability ...  
... of vaccines, ...  
... reluctance ...  
... to vaccinate, ...  
... and reduced effectiveness ...  
... of vaccination ...  
... against newly emerging variants underline the urgent need ...  
... for effective antivirals ...  
... (Saha et al., 2020).

**S2 [014]** The timeline of preclinical to clinical development of novel antivirals, however, is too long for completely new compounds to make a clinical impact during the current pandemic.

The timeline ...  
... of preclinical ...  
... to clinical development ...  
... of novel antivirals, ...  
... however, ...  
... is too long ...  
... for completely new compounds ...  
... to make a clinical impact ...  
... during the current pandemic.

**S2 [015]** Repurposing existing drugs with known safety profiles is, therefore, the most efficient and promising option.

Repurposing existing drugs ...  
... with known safety profiles is, ...  
... therefore, ...  
... the most efficient ...  
... and promising option.

**S2 [016]** Initial candidates, unfortunately, did not fulfill expectations (Cao et al., 2020; Horby et al., 2020).

Initial candidates, ...  
... unfortunately, ...  
... did not fulfill expectations ...  
... (Cao et al., 2020; ...  
... Horby et al., 2020).

**S2 [017]** Some other leads are still being tested in the clinic, but no convincing proof of efficacy has been provided as yet (Pan et al., 2020; Simonovich et al., 2020).

Some other leads are still being tested ...  
... in the clinic, ...  
... but no convincing proof ...  
... of efficacy has been provided ...  
... as ...  
... yet ...  
... (Pan et al., 2020; ...  
... Simonovich et al., 2020).

**S2 [018]** Importantly, it has been proposed that the identification of a set of antivirals against SARS-CoV-2 may provide an opportunity to mimic the strategy effective for HIV-1 - combinatorial treatment against different molecular targets (Lu et al., 2018).

Importantly, ...  
... it has been proposed ...  
... that the identification ...  
... of a set ...  
... of antivirals ...  
... against SARS-CoV-2 ...  
... may provide an opportunity ...  
... to mimic the strategy effective ...  
... for HIV-1 - combinatorial treatment ...  
... against different molecular targets ...  
... (Lu et al., 2018).

**S2 [019]** The coronaviral genome encodes several structural and non-structural proteins (Knipe and Howley, 2013), including two cysteine proteases, Mpro (nsp5) and PLpro (nsp3), essential for the virus replication (Shamsi et al., 2021).

The coronaviral genome encodes several structural ...  
... and non-structural proteins ...  
... (Knipe ...  
... and Howley, 2013), ...

## **End of Sample Audit**

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This is a truncated Manuscript Microscope Sample Audit.

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