BJMHR
British Journal of Medical and Health Research
Journal home page: www.bjmhr.com

The Twilight of Antibiotics: A predictive mathematical model of declining antimicrobial effectiveness, and a possible metabolic escape route.

E. Prieto Gratacós, J.A. Botto
Laboratorio de Ingeniería Biológica

ABSTRACT

Antibiotic resistance is increasing at a super-exponential rate worldwide. Design and approval of new antimicrobial compounds has sunk to the lowest levels in decades. At the current rate of decline in therapeutic effectiveness, the simultaneous emergence of multiple extensively resistant pathogens ("superbugs" or panresistant germs) is projected by this model to occur beyond a critical inefficacy threshold in approximately fourteen years (±3). Untreatable microbes will set back health services globally and will have a profound effect on medical disciplines that invariably need pharmacological control of opportunistic bacteria, such as Oncology and Transplantation medicine (that rely heavily on myelotoxic and/or immunosuppressive drugs), Odontology, Intensive Care, etc. No radically new categories of antibiotics have been discovered for decades. Combinatorial treatments that intend to accentuate antibiotic efficacy may even accelerate the rate of microbial adaptation due to increased selective pressure. Unless new categories of germicidal substances are developed, a reverse epidemiological transition seems inevitable. This paper describes our forecast based on a mathematical model from hard data on the declining effect of antimicrobial medication. Additionally, it suggests an already proven, scalable line of treatment that could overcome microbial resistance.

Keywords: Antibiotic resistance, super-exponential growth, ESKAPE pathogens, critical inefficacy threshold, enzymatic inhibition, structural analogs.

*Corresponding Author Name: E. Prieto Gratacós
Received 22 July 2026, Accepted 05 August 2026

Please cite this article as: Gratacós PE *et al*., The Twilight of Antibiotics: A predictive mathematical model of declining antimicrobial effectiveness, and a possible metabolic escape route. British Journal of Medical and Health Research 2026.

INTRODUCTION

Foundational epidemiology and global burden

Immediately prior to the SARS COV2 era, the global burden of deaths directly attributable to antimicrobial resistance (AMR) was already estimated to be about 1 million, annually (1-4). Recent studies provide hard-data evidence that antibiotic resistance is accelerating and currently killing well over a million. In underdeveloped nations, extra deaths are thought to be underreported or misclassified. AMR is not confined to developed countries with unrestricted access to antibiotics and large healthcare facilities, but rather a global phenomenon, with consistent reports emanating from virtually every region on Earth (5-7).

Also, demographic factors come into play as mounting population density in underdeveloped nations with overcrowded markets and hospitals of subpar hygiene standards facilitate colonization pressure. The ever-increasing number of asymptomatic carriers is considered a key epidemiological variable in the spread of antibiotic-resistant bacteria (ARB). It is well understood that colonization pressure drives adaptation, especially in healthcare settings like ICUs, but also in massive social gatherings such as fairs and music festivals. Higher colonization pressure directly increases the likelihood that non-colonized patients will acquire the resistant bacteria through cross-transmission. As such, it has been linked to the spread of MRSA, CRAB, CRPA, XDR-*K. pneumoniae*, and VRE (detailed nomenclature given below) (9). Given present-day population dynamics and global interconnectedness, colonization pressure amplifies resistance transmission horizontally beyond individual-level antibiotic exposure (10).

Across the board, the latest global burden work uniformly suggests AMR-attributable deaths continue to rise at present, with ~1.91M annual deaths by 2040 and tens of millions of deaths over 2025–2050 if no strong, conceptually new intervention occurs. *Exempli gratia*, carbapenem-resistant deaths are projected to escalate sharply by 2035 even as overall age-standardized mortality declines, showing increasing resistance intensity in key pathogens (10).

Exponentially evolving pan resistant strains

Without exception, from *Mycobacterium tuberculosis to Neisseria gonorrhoeae,* any and all microbes subjected to selective pressure under germicidal substances are evolving in a significant manner. Amongst the most frequently cited pathogens in the literature are *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter*, cleverly designated under the acronym ESKAPE (and later added, *Escherichia coli, rendering ESKAPEE)*. Dozens of papers

stemming out of multiple countries report longitudinal hard-data trends in resistance and antibiotic usefulness concerning pathogens on the ESKAPE cluster (11).

All classes of bacterial pathogens express a similar tendency towards adaptability and survival, showing highly dynamic susceptibility patterns (13,14). Amongst many hundreds of reports, a rather large retrospective cohort study based on a 7-year dataset comprising 190.000 subjects showed an upward trend in AMR detection despite stable antibiotic use intensity (12). Ubiquitously, rising resistance among Gram-negative pathogens to 3rd-gen cephalosporins and carbapenems post-2020 is also documented worldwide (15-20). Autoregressive integrated moving average (ARIMA) models linking monthly antibiotic use intensity to resistance trends lead to the same conclusion, showing quantitively how carbapenem-resistant and 3rd-gen cephalosporins-resistant strains increase mortality vs susceptible strains (21).

Over recent years some efforts have been made to preserve antibiotic efficacy, to no avail. Different antibiotic-cycling strategies affect resistance evolution, but selective pressure simply forces a "Darwinian" adaptation (22). Proper diagnostics through lab tests (cultivation) as opposed to indiscriminate prescription, as well as taking the treatment to completion have made at best a modest dent in the progression of the general loss of antimicrobial efficacy. Given its universal upward trend, the inevitability of the emergence of panresistant germs is now evident. As referenced here, a host of peer reviewed studies deal explicitly with "superbugs", including Methicillin-resistant *Staphylococcus aureus* (MRSA), Carbapenem-resistant *Acinetobacter baumannii* (CRAB), Carbapenem-Resistant *Pseudomonas aeruginosa* (CRPA), Extensively Drug-Resistant (XDR)-*Klebsiella pneumoniae*, and Vancomycin-resistant enterococci (VRE) (23-36).

MATERIALS AND METHOD

Programming tools and open computational companion

The quantitative claims of this paper rest on a multi-source synthesis: more than ten peer-reviewed sources for the resistance trajectory, three independent mortality streams (GRAM/O'Neill, Murray 2022, Tai 2025), a per-pathogen surveillance matrix spanning four global agencies (WHO GLASS, ECDC EARS-Net, CDC AR Threats, Murray 2022) and a complementary SARIMA exercise. The data on mathematical and population-level models of AMR was harvested from the repositories PubMed, EMBASE, and The Cochrane Library by means of advanced search features of www.Perplexity.ai

Static figures alone do not let the reader inspect the anchor points individually, re-evaluate the calibration milestones, or visualize alternative parameterizations of the super-exponential model. We therefore developed an open computational companion that exposes every model

surface, every anchor table and every calibration coefficient to direct inspection. This decision follows the FAIR Principles for Research Software (Chue Hong et al., 2022) and the Force11 Software Citation Principles (Smith et al., 2016), which together establish that software underpinning quantitative claims should be findable, accessible, openly licensed and citable as a first-class research output.

Implementation

The companion is a multi-page interactive application implemented in Python 3.12. NumPy and pandas drive the closed-form models; stats models perform the SARIMA fits; and the rendering layer is built on Plotly and Dash. The application runs as a single self-contained Python process and requires no external API at run-time —every coefficient and every anchor point is embedded in the source— so it can be served as a public web instance or executed offline from a local clone with identical results.

Components

The application is organized in ten pages that mirror the structure of this paper:

- An Overview page that plots the super-exponential resistance trajectory against the constant-rate reference logistic, with the published anchor points overlaid and the critical-point window 2040 – 2047 highlighted;
- A Pathogens page that renders the ESKAPEE × antibiotic-class surveillance matrix together with WHO priority labels and Magiorakos (2012) isolate-level phenotype badges, plus regional and temporal-trend panels;
- A Time Series page that fits SARIMAX(1,1,1)(1,1,0,12) models on monthly resistance series with ACF/PACF correlograms, residual diagnostics, AIC/BIC reporting and a counterfactual intervention scenario;
- An Industry page covering bibliometric growth (PubMed search “antibiotic resistance”, 1990–2025), the antibiotic-resistance market trajectory (Univdatos CAGR 5.4 % through 2032), and the awareness-versus-effectiveness divergence discussed in the body of this paper;
- A Metabolic page that scaffolds the antimetabolic line of treatment at a conceptual level;
- Data Sources, References, Export Studio, Documentation and Tutorial pages that complete the editorial perimeter —fully cited source list with direct links, a publication-grade figure-export workspace and onboarding material for first-time users.

Access and licensing

The source code is released under an open-source license and will be deposited in a long-term archive (Zenodo) with a citable DOI at the time of publication; quoted here in the camera-ready version. Following the Force11 Software Citation Principles, we ask that any reuse of the model coefficients, anchor tables or visualizations cite the deposited release rather than this paper alone. The application is publicly available at https://resistome.imhoit.com

Reproducibility

The central super-exponential forecast is implemented as a closed-form analytic expression with hand-calibrated coefficients; no parameter fitting, no random sampling and no Monte Carlo are involved. Mortality and pathogen surveillance values are loaded from named published sources and presented as such, not derived from the resistance-pressure model. The SARIMA series are generated deterministically with a fixed seed to guarantee that the diagnostic plots reported in the companion can be reproduced identically across machines. Together these design choices ensure that every figure in this paper can be re-derived bit-for-bit from the open source — a property that the FAIR4RS framework treats as the minimum bar for research software supporting publication.

Citation of the companion

Prieto Gratacós, E. & Botto, J. A. (2026). The Twilight of Antibiotics —open computational companion [Software]. Zenodo. DOI: [to be assigned at publication]. Available at https://resistome.imhoit.com

Forecast segment (2026–2060) and critical inefficacy threshold

Admitting a degree of uncertainty of ±3 years, we surmise that in the period 2025-2032 resistance pressure grows from ~70 to ~80. Through the following period, 2033-2040, resistance steepens to ~90. Whereas 2040-2047 sees a curve that approaches ~95–98, interpreted as the critical inefficacy threshold, with new drugs only temporarily delaying the asymptote. The implications of reaching critical inefficacy are vast, since by that time many first-line antibiotics are utterly useless for nosocomial Gram-negative infections. It appears inevitable to these authors that, within that interval, carbapenem-resistant and several panresistant “superbugs” become common, rather than exceptional. Finally, in our model, within the 2045–2060 period the curve slowly approaches ~100: near-total ineffectiveness of virtually all classes of antibiotics.

A note on bibliometric dynamics and industry trends:

It is worth noting, as a measure of collective professional awareness, that a scientometric assessment of this phenomenon (as per the search terms “antibiotic resistance”) does indeed show an increase in recognition within the community (image #4) (37). However, research and development (R&D) investments have been decelerating, currently at 5.4% compound

annual growth rate (CAGR), a pace clearly insufficient relative to the pervasive loss of germicidal power (image #5) (38). Through the lens of our own forecast, both awareness and action seem ineffectual. Although the antibiotic resistance market has been evolving on par with the declining effect of standard pharmaceuticals, no increase in efficacy is apparent. This divergence has been designated by the medical community as the antibiotic "choke point", to which no solution has so far been discernible within the antibiotic paradigm.

Image #1 Super-exponential model of the Antimicrobial Resistance Pressure index (1990-2060), with critical inefficacy threshold. https://resistome.imhoit.com

Image #2 Projected AMR-induced mortality according to three distinct methodologies. https://resistome.imhoit.com

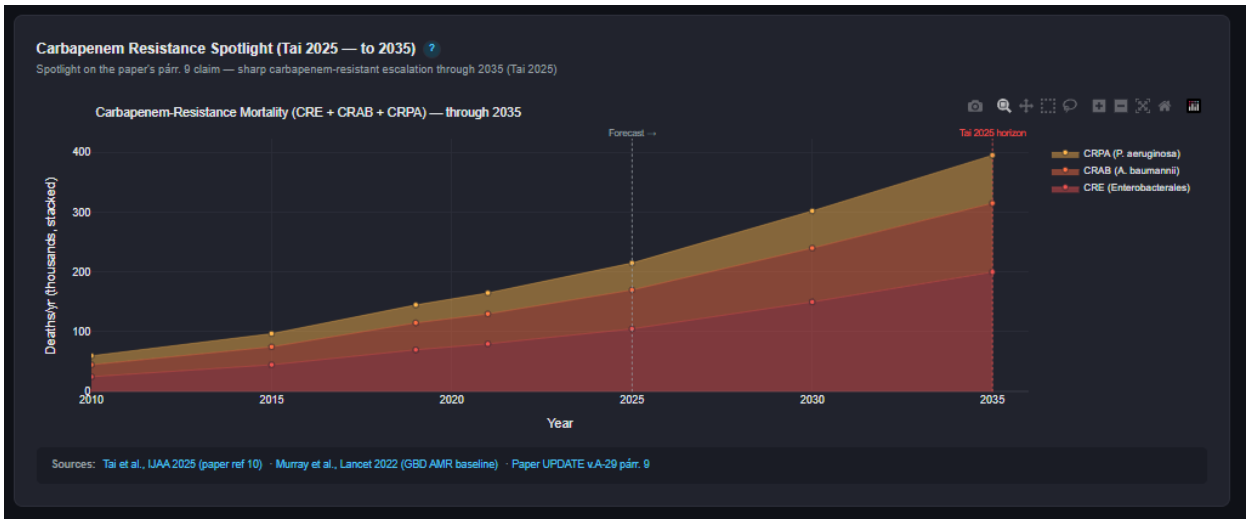

Image #3 Projected mortality from carbapenem-resistant *P. auriginosa, A. baumanii and Enterobacter*. https://resistome.imhoit.com

Image #4 Published peer-reviewed papers on "antibiotic resistance" from www.PubMed.Gov, cumulative results up to 2025. https://resistome.imhoit.com/industry

Image #5 a) Compound annual growth rate (CAGR) of the Antibiotic Resistance Market. b) Expected market size by drug class. https://resistome.imhoit.com/industry

DISCUSSION

In the scientific literature at large, which includes studies on a vast array of pathogens, germicidal substances, countries, and installations (ICUs, nurseries, hospitals, animal farms), interpretation of the AMR phenomenon has been tackled from every possible angle. Some integrate within-host and between-host dynamics of resistance (39-41), some take a population-level approach, some relay on volume of medication and/or time needed to treat. Regardless of the emphasis, exponential increase in antibiotic resistance is seemingly universal, but assumed to be discrete ($V=Sx(1+r)^T$, the only difference being the passage of time (T), taken as the true exponent, given a fixed rate of pathogen adaptation capability (*r*). Our analysis considers that the rate of increasing resistance is itself growing, which better suits a continuous growth model $P=P_0 \cdot \exp^{(r \cdot t)}$. In our computational companion, however, we have implemented a generalized logistic with a quadratic exponent $y(\tau)= K / [1 + A \cdot \exp^{(-r \cdot \tau - b \cdot \tau^2)}]$, which makes for a mathematically stronger model, adding saturation ceiling at K and a time-varying rate. The $-b \cdot \tau^2$ term is the minimal closed-form way of expressing a rate that grows linearly in time, while the K factor encodes the biological ceiling.

Note: The resistance index is bounded above by 100% by construction, so an unbounded $P = P_0 \cdot \exp^{(r \cdot t)}$ would diverge past the biological ceiling. The logistic envelope is a necessary -not a decorative- choice. And once a saturating envelope is present, adding the $-b \cdot \tau^2$ term in the exponent is exactly the formal expression of the thesis "the rate is itself growing."

Taking an average of the strongest sources available -including O'Neill-style projections, GRAM-type forecasts, and Lancet-GBD-style analyses- we have constructed a forecasting model that allows for a stronger predicting value. This approach suggests a grimmer prospect for healthcare in general, since adjudicating a greater influence to *r* compresses the time lapse

necessary to reach critical inefficacy. Reproducibility of the model is readily feasible from the companion software.

Limitations

This model carries several limitations that bound its interpretation; stating them explicitly reflects deliberate methodological choices and constraints inherent to the field, rather than shortcomings of the implementation. First, the resistance-pressure index is a normalized composite (0–100): it is a standard methodological device for synthesizing heterogeneous indicators into a comparable, fully transparent and reproducible scale, not a directly measured quantity. Second, the coefficients of the generalized logistic are anchored to published milestones rather than fitted statistically; this is a deliberate choice to avoid overfitting noisy surveillance data and to guarantee bit-for-bit reproducibility, and the out-of-sample back-validation (calibrated on pre-2016 data alone) confirms that the model generalizes, predicting 2019–2025 within approximately four index points and conservatively. Third, the SARIMA exercise is run on a synthetic monthly series: this reflects the absence of openly harmonized monthly per-pathogen series in the literature —not a design shortcoming— and the same procedure runs unchanged on real series as they become available. Fourth, the underlying surveillance data carry well-documented biases —clinical isolates overestimate population-level resistance, geographic coverage is uneven, and laboratories differ in breakpoint standards (EUCAST vs. CLSI)—; these are universal limitations shared by every global-burden estimate of AMR (Murray/GBD, O'Neill), and acknowledging them is standard practice. Finally, the critical inefficacy threshold (~95) is operationalized from clinical breakpoints in the absence of an external consensus cut-off, and is presented transparently as a provisional construct. Taken together, these considerations do not alter the paper's central thesis —that the rate of resistance is itself increasing— but they frame the precision attributable to any specific date or index value.

Antimetabolites in the treatment of infections

As a working hypothesis, we propose now that a readily accessible, non-toxic approach to overcoming antibiotic resistance could be the enzymatic disruption of bacterial metabolic pathways with structural analogs of glucose (39-42). This kind of antimetabolic interventions has been known for decades, since it is based on the principle of competitive inhibition (43). *In vivo,* enzymatic inhibition with structural analogs (EISA) is only possible due to the pronounced functional asymmetry between normal eukaryotic cells and bacteria. Many ESKAPE pathogens behave as facultative anaerobes, relying heavily on transporters and fermentation pathways functionally equivalent to the GLUT family, and to hexokinase-2 and LDH-A, respectively, all of which are demonstrably susceptible to competitive inhibition

(44-46). Although their glucose-uptake and metabolism are mechanistically distinct from their mammalian counterparts, they share enough biochemical architecture to be susceptible to the same class of structural-analog inhibitors that have long been characterized in oncology.

Antimetabolites such as 2-deoxy-D-glucose (2DG) -an undegradable pseudo-sugar with antiproliferative effects- and sodium ascorbate (a six-carbon glucose analog) have proven both safe and effective for the treatment of cancer and opportunistic infections in humans (47, 48). Ascorbate is widely recognized for its strong antimicrobial and antineoplastic properties, when applied in pharmacological doses through the intravenous route (49,50). Said effects are enhanced by means of the synchronous use of autophagy inhibitors such as hydroxychloroquine (51-53). Interestingly, antimetabolic interventions that constrict bacterial access to biosynthetic material and energy sources have retained their efficacy over the decades. A probable explanation of this phenomenon seems to be that rapidly growing bacteria cannot overcome deep, extended starvation (54). Based on this general principle, non-toxic antimetabolites should be tested clinically, as a means to neutralize bacterial infections.

Funding: All funds required for the research, writing and publication of this paper have been provided entirely by the authors.

Conflicts of Interests: As of this writing, the authors have no competing interests (directly or indirectly, by ownership or by affiliation) with any brand, company, or institution. No outside contributors had any role in the design, implementation, or analysis of the study or the write-up of this paper.

REFERENCES

1- Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Murray, C. J. L. et al. Lancet 399, 2022.
2- Global burden of bacterial antimicrobial resistance in 2019: summary and implications. BMJ (2022).
3- Aslam, B. et al. Antibiotic Resistance: One Health One World Outlook. Front. Cell. Infect. Microbiol., 2021; O'Neill, J. Review on Antimicrobial Resistance.
4- DalBen, M. F. et al. A Model-Based Strategy to Control the Spread of Carbapenem-Resistant Enterobacteriaceae: Simulate and Implement. Infect Control Hosp Epidemiol. 2016;37(11):1315-1322. doi: 10.1017/ice.2016.168.
5- Multidrug-Resistant Bacteria in the Community: Trends and Lessons Learned." Van Duin, D. & Paterson, D. L. Infect. Dis. Clin. North Am., 2016.

6- Antimicrobial use, healthcare-associated infections, and bacterial resistance in general hospitals in China: the first national pilot point-prevalence survey report." Eur. J. Clin. Microbiol. Xiao, Y. et al. Infect. Dis., 2023.

7- Patterns of multi-drug resistant bacteria at first culture from patients admitted to a third-level university hospital in Calabria from 2011 to 2014. Reale, M. et al. Infez. Med., 2017.

8- Risk Factors for Gastrointestinal Colonization and Acquisition of Carbapenem-Resistant Gram-Negative Bacteria among Patients in Intensive Care Units in Thailand Antimicrob Agents. Anong Kiddee *et al*. Chemother. 2018

9- Colonization pressure: a critical parameter in the epidemiology of antibiotic-resistant bacteria. Bonten, M. J. M. Crit. Care, 2012.

10- Global, regional, and national burden of bacterial carbapenem resistance from 1990 to 2021 and predictions up to 2035. Jie-Hao Tai, Yi-Le Wu et al. Int J Antimicrob Agents doi: 10.1016/j.ijantimicag.2025.107636.

11- ESKAPE pathogens: antimicrobial resistance, epidemiology, clinical impact and therapeutics | Nature Reviews Microbiology. William R. Miller & Cesar A. Arias. Nature Reviews Microbiology volume 22, pages598–616 (2024)

12- Epidemiological investigation and patterns of antimicrobial use in multidrug-resistant bacteria at a tertiary hospital: a retrospective cohort study. Man Wang, Qiang Fu. BMJ Open doi: 10.1136/bmjopen-2025-099847

13- Predicting antimicrobial resistance of bacterial pathogens using time-series data from >600 farms. Kim, J. et al. Front. Microbiol., 2023.

14- Time series analysis of antibacterial usage and bacterial resistance in China: observations from a tertiary hospital from 2014 to 2018. PLoS One, 2019.

15- Impact of carbapenem resistance on mortality in patients infected with Enterobacteriaceae: a systematic review and meta-analysis. Zhou, R. et al. BMJ Open, 2021.

16- Clinical epidemiology of carbapenem-resistant Enterobacterales in the Greater Houston region of Texas: a 6-year trend and surveillance analysis. Tadese, B. K. et al. J. Glob. Antimicrob. Resist., 2022.

17- Surveillance of carbapenem-resistant Klebsiella pneumoniae in Chinese hospitals – A five-year retrospective study. Qu, X. et al. J. Infect. Dev. Ctries., 2019.

18- Carbapenem-Resistant Klebsiella pneumoniae in Large Public Acute-Care Healthcare System, New York, New York, USA, 2016–2022. Lee, J. et al. Emerg. Infect. Dis., 2023.

19- Healthcare-associated carbapenem-resistant Klebsiella pneumoniae infections are associated with higher mortality compared to carbapenem-susceptible K. pneumoniae infections in the intensive care unit. Yao, Y. et al. J. Hosp. Infect., 2024.

20- Epidemiology of carbapenem-resistant Enterobacteriaceae. Chotiprasitsakul, D. et al. Infect. Drug Resist., 2019.

21- Chatzopoulou M, Reynolds L. Systematic review of the effects of antimicrobial cycling on bacterial resistance rates within hospital settings. Br J Clin Pharmacol. 2022;88(3):897-910. doi:10.1111/bcp.15042

22- Antibiotic Cycling Affects Resistance Evolution Independently of Collateral Sensitivity. Brepoels P, Appermans K, Pérez-Romero CA, Lories B, Marchal K, et al. Mol Biol Evol. 2022 Dec 5;39(12):msac257. doi:10.1093/molbev/msac257. (Open access via PMC: PMC9778841).

23- Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions. Magiorakos, A. P. et al. Clin. Microbiol. Infect., 2012.

24- Carbapenem-resistant *Enterobacteriaceae*: epidemiology and management. E. Temkin, A. Adler, A. Lerner, Y. Carmeli Clin. Microbiol. Rev., 2014. DOI: 10.1111/nyas.12537

25- Carbapenem-resistant *Klebsiella pneumoniae*: a global threat. Expert Rev. Anti-Infect. Ther., 2020.

26- Molecular and clinical epidemiology of carbapenem resistant Acinetobacter baumannii ST2 in Oceania: a multicountry cohort study. S. C. Baleivanualala, S.V. Devi, B. Howden, C.L. Gorrie, S. Matanitobua et al. Lancet Inf Dis. 2017.

27- Carbapenem-resistant Pseudomonas aeruginosa. Front. Microbiol., 2019.

28- Methicillin-resistant Staphylococcus aureus (MRSA): a global perspective. Lancet Infect. Dis., 2016.

29- Vancomycin-resistant Enterococcus (VRE): epidemiology and outcomes. Clin. Microbiol. Rev., 2019.

30- Pandrug-resistant Acinetobacter baumannii: emergence and clinical implications. J. Infect., 2018.

31- Pandrug-resistant Gram-negative pathogens in the ICU. Crit. Care, 2021.

32- Pan-drug-resistant Pseudomonas aeruginosa: a case report and review. J. Infect. Public Health, 2019.

33- Extensively drug-resistant tuberculosis (XDR-TB): global epidemiology. Lancet, 2018.

34- Pandrug-resistant Klebsiella pneumoniae producing carbapenemases in a European ICU. Antimicrob. Agents Chemother., 2020.

35- Pandrug-resistant Enterobacter spp. in a teaching hospital. J. Glob. Antimicrob. Resist., 2021

36- Extensively drug-resistant Stenotrophomonas maltophilia in a tertiary care hospital in Taiwan: microbiologic characteristics, clinical features, and outcomes. Che-Kim Tan et al. Diagnostic Microbiology and Infectious Disease, 2008 10.1016/j.diagmicrobio.2007.09.007

37- https://pubmed.ncbi.nlm.nih.gov/?term=antibiotic+resistance

38- Antibiotic Resistance Market: Current Analysis and Forecast (2024-2032). https://univdatos.com/reports/antibiotic-resistance-market

39- Inhibition of sugar uptake by ascorbic acid in Escherichia coli. Loewen PC, Richter HE. Arch Biochem Biophys. 1983;226(2):657–665.

40- Alternate pathway to ascorbate induced inhibition of Mycobacterium tuberculosis. Shukla H, Tripathi A, Shukla S. Tuberculosis (Edinb). 2018;111:161–169.

41- 2-Deoxy-D-glucose is a potent inhibitor of biofilm growth in Escherichia coli. Hoffman PS, et al. Microbiology. 2016;162(6):1037–1046.

42- Regulation of glycolysis and sugar phosphotransferase activities in Streptococcus lactis: growth in the presence of 2-deoxy-D-glucose. Thompson J, Chassy BM. J Bacteriol. 1982;149(1):183–193.

43- Antimetabolites in the Treatment of Solid Tumors: Competitive Inhibition by Structural Analogs. Prieto Gratacós, Ernesto. Journal of Oncology Research and Therapy, 2026. doi:10.29011/2574-710X.10342.

44- Activity of the Lactate Dehydrogenase Inhibitor Oxamic Acid against the Fermentative Bacterium Streptococcus mitis/oralis: Bactericidal Effects and Prevention of Daptomycin Resistance. R. Kebriaei et al. Antibiotics, (2022) DOI: 10.3390/antibiotics11101409

45- Energy Conservation in Fermentations of Anaerobic Bacteria. Wolfgang Buckel. Frontiers in Microbiology, (2021) DOI: 10.3389/fmicb.2021.703525

46- Kinetic characterization of annotated glycolytic enzymes present in cellulose-fermenting Clostridium thermocellum suggests different metabolic roles. S.R. Daley et al. Biotechnology for Biofuels and Bioproducts, (2023) DOI: 10.1186/s13068-023-02362-8

47- Safety of Antimetabolite 2-Deoxy-D-arabinohexose (2DG) as a Coadjuvant Metabolic Intervention in 268 Cancer Patients. Prieto Gratacós E. Cancer Medicine Journal. 2020;

48- The wonders of 2-deoxy-D-glucose. Xi J, et al. IUBMB Life. 2014;66(2):73–80.

49- Evaluation of antibacterial activity of vitamin C against human bacterial pathogens. Braz J Biol. 2021;82:e243836.

50- Reversal of the Pathophysiological Responses to Gram-negative Sepsis by Megadose Vitamin C** by Y.R. Lankadeva et al. Critical Care Medicine, (2021) DOI: 10.1097/CCM.0000000000004778

51- Chloroquine Inhibits Autophagy, Enhances p53-Dependent Apoptosis, and Delays Tumor Recurrence in a Mouse Model of B Cell Lymphoma. RK. Amaravadi, A. Thomas-Tikhonenko, CB. Thompson. Blood 2005. doi.org/10.1182/blood.V106.11.2421.2421

52- The clinical value of using chloroquine or hydroxychloroquine as autophagy inhibitors in the treatment of cancers: A systematic review and meta-analysis. Xu, Ran; Ji, Ziyi; Xu, Chen; Zhu, Jing MD. Medicine, 2018. DOI: 10.1097/MD.0000000000012912

53- Hydroxychloroquine inhibits autophagy to potentiate antiestrogen responsiveness in ER+ breast cancer. Cook KL, Wärri A, Soto-Pantoja DR, Clarke PA, Cruz MI, Zwart A, Clarke R. Clin Cancer Res. 2014 doi: 10.1158/1078-0432.CCR-13-3227.

54- Targeting metabolism to combat anticancer and antibacterial drug resistance. https://doi.org/10.1016/j.tips.2026.01.013
CH. Chung, R. Bhowmick, AJ. Badenoch, HS. Arora, S. Chandrasekaran. Trends in Pharmacological Sciences, 2026.

55- Metabolic state-driven nutrient-based approach to combat bacterial antibiotic resistance. Bo Peng, Hui Li, Xuan-xian Peng. NPJ Antimicrob Resist,2025 doi: 10.1038/s44259-025-00092-5