Bioinformation Volume 5 *open access*

www.bioinformation.net Issue 8 **Database**

The Antimicrobial Index: a comprehensive literature-based antimicrobial database and reference work

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Received December 15, 2010; Accepted December 27, 2010; Published January 22, 2011

Abstract:
Although the ever-growing usage of antimicrobials in the fields of medicine, pharmacology, and microbiology have undoubtedly allowed for unprecedented advances in the scientific world, these advances are nevertheless accompanied by unprecedented challenges. Sharp increases in antibiotic usages have led to inefficient and wasteful usage practices. Bacterial resistances have dramatically increased and therefore hindered the effectiveness of traditional antibiotics, thus forcing many life-science professionals to turn to plant extracts and synthetic chemicals **[1]**. The Antimicrobial Index (TAMI) seeks to alleviate some of these mounting difficulties through the collection and centralization of relevant antimicrobial susceptibility data from journals. Data compiled for antimicrobials include: method of action, physical properties, resistance genes, side effects, and minimal inhibitory concentrations (MIC50, MIC90 and/or ranges). TAMI currently contains data on 960 antimicrobials and over 24,000 microorganisms (3,500 unique strains) which were collected from over 400 pieces of published literature. Volume and scope of the index have been and will continue to increase and it is hoped that such an index will further foster international cooperation and communication of antimicrobial-related knowledge. TAMI can be accessed at: http://antibiotics.toku-e.com/.

Background:
It is well known that there is a direct correlation between the increases in worldwide usage of antimicrobial agents and microorganism resistances **[2]**. Patients infected by various highly resistant bacteria and/or fungi, leave no choice to physicians other than in inundate the bacteria/fungi with highly potent antimicrobial agents. Treatments such as these not only lead to super-resistant bacterial strains, but essentially render once deemed "highly potent" antibiotics useless. Furthermore, over the past decades, this surge in resistances has directly stimulated rigorous research in the field of antimicrobial susceptibilities. The universal metric used to perform antimicrobial susceptibility potency tests is the minimum inhibitory concentration (MIC), which is usually measured in units of (μg/ml) **[3]**. It is important to note that during susceptibility testing, some authors prefer to provide zone of inhibition (mm) readings alongside MIC results, but such data is not ubiquitous and therefore not included in the database.

Another pressing challenge facing the scientific community is the lack of comprehensive and centralized data on the specific methods of action of antimicrobial agents. Data such as methods of action, physical properties, and resistance genes for commonly used antimicrobials such as vancomycin, penicillin, and ampicillin are readily available from various sources. But with increasingly emerging resistances worldwide, the scientific community needs a deeper understanding of the methods of actions of other, traditionally overlooked or even newly discovered agents. Surprisingly, the literature contains hundreds of either traditionally overlooked or recently discovered antimicrobial agents which often times hold promise in their lower MIC values. Through a wide collection of susceptibility data, TAMI seeks to alleviate some of the aforementioned challenges and ultimately seeks to foster international communication and cooperation in research, discovery and most importantly the use of antimicrobial agents.

Methodology:
Construction of TAMI:
The susceptibility data in TABI was inputted, sorted, and eventually published in both print and digital form. Data was collected from dozens of journals including: Antimicrobial Agents and Chemotherapy, International Journal of Antimicrobial Agents, Journal of Medicinal Chemistry, Diagnostic Microbiology and Infectious Disease, and European Journal of Pharmaceutical Sciences. Specific testing methods such as BSAC agar dilution, BSAC disk diffusion, NCCLS broth micro-dilution, Etest strips, etc. were generally omitted except in cases where data was deemed significantly different **[4]**. Due to the inconsistency in nomenclature of antimicrobial agents and strains, names which are no longer used have been standardized in the data **[5]**. TAMI's high volume of data overcomes this challenge by providing abundant data for the user to deem what data points fall as outliers. Google Scholar **[6]** was utilized for sorting and indexing of papers. The electronic, web-based version of the database is written in C+ and can be accessed at http://antibiotics.toku-e.com/. **Figure 1** shows process for collection and refining of data.

Features:
TABI contains 960 antimicrobial agents, 24,000+ microorganisms (3,500 unique strains) and over 400 journal articles. Basic information for many of the contained antimicrobials such as methods of action, physical data, and resistance genes are included therein. The search function allows for searches to be performed by any of the following criteria: antimicrobial name, microorganism name, strain designation (ex. ATCC#), and strain resistances (methicillin- resistance). Interactive clickable links for related and relevant antimicrobials and microorganisms allow for cross-referencing of MIC data.

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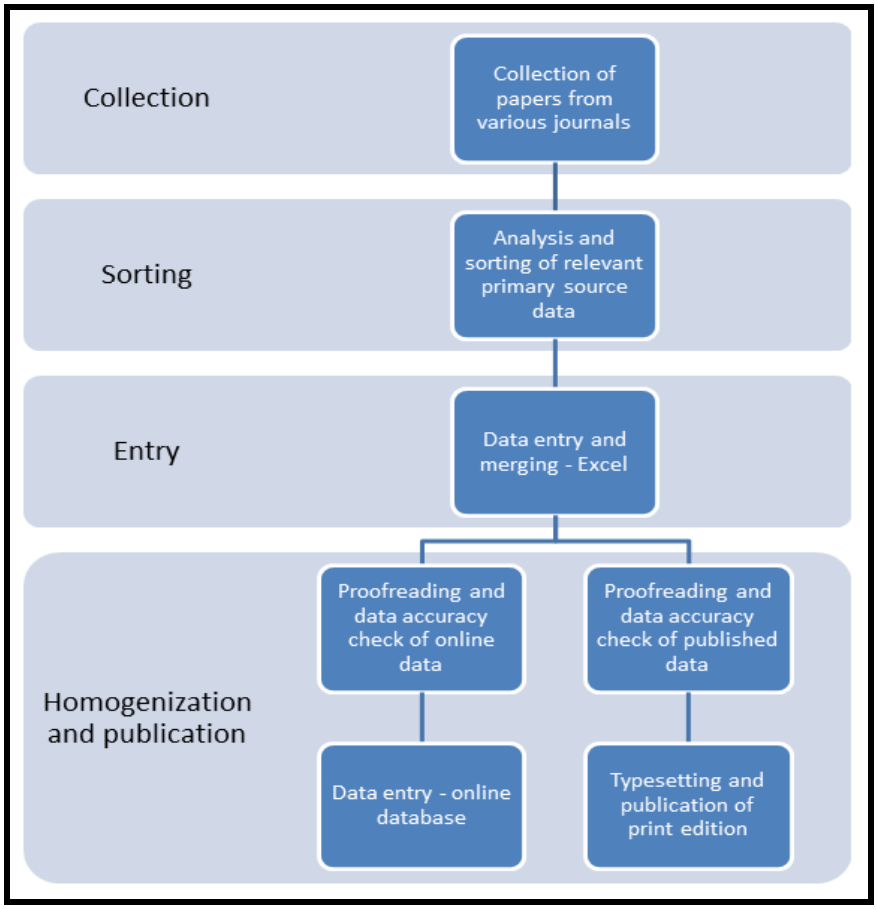

Figure 1: Flowchart of construction of The Antimicrobial Index. Papers were primarily found through using MIC relevant keywords in Google scholar such as: antimicrobial, in vitro, MIC, and µg/ml. Data sorting and filtration comprised of omitting irrelevant data such those pertaining to susceptibility percentages, overly complex experimental and/or synthetically prepared compounds, time-kill studies, and other non-MIC data. Errors and nomenclature variations in the primary text data became increasingly apparent through the entry, merging, and sorting of data in Microsoft Excel. Errors such as microorganism or antimicrobial misspellings were revised. Unit differences were standardized to µg/ml. Refined data was subsequently published into the online and print versions of TAMI.

Utility to the Greater Biological Community:

Although TABI can be used by and can benefit a diverse range of people, microbiologists, cell biologists, life-science professionals will in particular find the database useful. In addition to being able to confirm data, the database can be used to introduce other more effective antimicrobials and/or literature resources to the user. Furthermore, by knowing an approximate range of antimicrobial concentrations, the user can economize in the purchasing of their needed antimicrobial agent and more importantly, a reduction in usage will lead to a decreased spike in the ever-growing resistance levels of microorganisms **[7]**.

Future Directions:

Although TAMI's scope and content have exceeded previous attempts at creating susceptibility databases, in its current state TAMI serves as an initial tool which is developing into a world-class database **[8]**. The editorial board plans to double the number of papers to more than 800 in the next year and continue expansion at a pace of at least 100 additional papers/ month thereafter. Work on expanding the distribution of TAMI through various feedback channels is already underway and content is steadily being expanded.

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Edited by W Perrizo

Citation: **Amirkia & Qiubao,** Bioinformation 5(8): 365-366 (2011)