Bayode *et al.*
Bulletin of the National Research Centre (2022) 46:149
https://doi.org/10.1186/s42269-022-00841-w

Bulletin of the National Research Centre

REVIEW

Open Access

Isothermal microcalorimetry (IMC) calscreener: automated peculiarities of antimicrobial therapy and metabolism depth of multidrug resistant bacteria

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Abstract

Background: The global development of innovative antimicrobial drugs and drug design techniques has been necessitated by the persistent increase of multidrug resistant infections. Regardless of advances in technology for detecting pathogenic bacteria and their resistance genes (DNA-based assays), most bacteriological studies of infections still use conventional cultural techniques and susceptibility testing as reference standards. Commonly used conventional assays such as the disc diffusion test and broth micro-dilution have been effective in defining pathogen susceptibility and determining the minimum inhibitory concentration of antimicrobial agents. However, they are still prone to error and time consuming, hence, not sufficient in the face of the urgent need for answers to sporadic worldwide disease maladies.

Main body: In this review, we describe a developing but promising method for gauging/measuring the amount of energy released when a cell is actively metabolizing, which may then be used to calculate the bacterial cell's growth rate. The isothermal microcalorimetry (IMC) calscreener translate heat production of cellular metabolism which is pertinent to the operation of all biological life in demonstrating a more advanced technique for drug design and discovery, especially in the area of pathogen-specific chemotherapy.

Conclusion: The IMC calscreener technology is sacrosanct in establishing the heat levels in microwatt to read the metabolic kinematics of biological specimens with emphasis on medically-relevant bacteria within a closed scheme. The application of this technology also looks promising in antimicrobial chemotherapy and metal recovery.

Keywords: Multidrug resistant (MDR) infections, Disc diffusion test (DDT), Broth micro-dilution (BMD), IMC calscreener, Heat production, Metabolism

Background

The swift establishment of the cause/origin of a microbial infection and commencement of pathogen-specific chemotherapy stands as the key foundation for the effective treatment of infections. Even with the advancement in technology engaged in the detection of pathogenic microorganisms and their resistant genes (DNA-based assays), the conventional cultural techniques and susceptibility testing are still employed as reference for bacteriological studies of infections (Tellapragada et al. 2020). Commonly used conventional assays by laboratories globally are disc diffusion test (DDT) and broth micro-dilution (BMD) assays for

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defining the susceptibility of the pathogens and determination of the minimum inhibitory concentration (MIC) of antimicrobial agents.

Minimum inhibitory concentration determination of available drugs and novel antimicrobial agents is necessitated by the increase of multidrug resistant (MDR) pathogens globally. Some existing systems for automated determination of pathogen susceptibility and MIC are not error-free when compared to the results obtained from BMD (Haffler et al. 2019; Matuschek et al. 2018). Besides, a large proportion of these automated systems require incubation for as long as 18 h to give results which are roughly the amount of time required when using the conventional DDT and BMD (Tellapragada et al. 2020). It therefore remains a major task for medical laboratories globally to adopt methods that will provide dependable antimicrobial susceptibility and MIC results in a short time interval, which will strengthen winning the battle against MDR pathogens.

As a rider to these observations, the isothermal microcalorimetry (IMC) calscreener has gained prominence for gauging/measuring the amount of energy given off when a cell is actively metabolising, which in turn can be used to measure the growth rate of the bacterial cell. The application of IMC calscreener is grounded in its ability to measure the energy given off in an isothermal, closed system in microwatt (μW), making it a budding technique in assaying the growth rate of bacteria with respect to the concentration of substrate availability (Butini et al. 2019; Braissant et al. 2010). Some of the advantages of IMC calscreener over conventional assay methods for susceptibility testing include increased sensitivity, thereby increasing the propensity for early detection of resistance or inhibition and also allows for testing under varying conditions (including aerobic and anaerobic conditions). This technique has also been employed to study how antimicrobial agents acts when used at minimal concentrations (von Ah et al. 2009). This review focuses on the automated peculiarities of the in-vivo and in-vitro antimicrobial therapy and metabolism measurement of multidrug resistant bacteria using the IMC calscreener. A schematic framework of the utilization of the IMC calscreener for metabolism heat production measurement of biological specimens comprising microbes, aerobic specimens and anaerobic specimens in real time is illustrated in Fig. 1.

Main text

The working principle of the isothermal microcalorimetry calscreener: dynamics between biological metabolism and heat production

One of the best ways to assess the decrease or increase in the microbial population in a culture system is by the direct assessment of the metabolic rate. Based on the fact

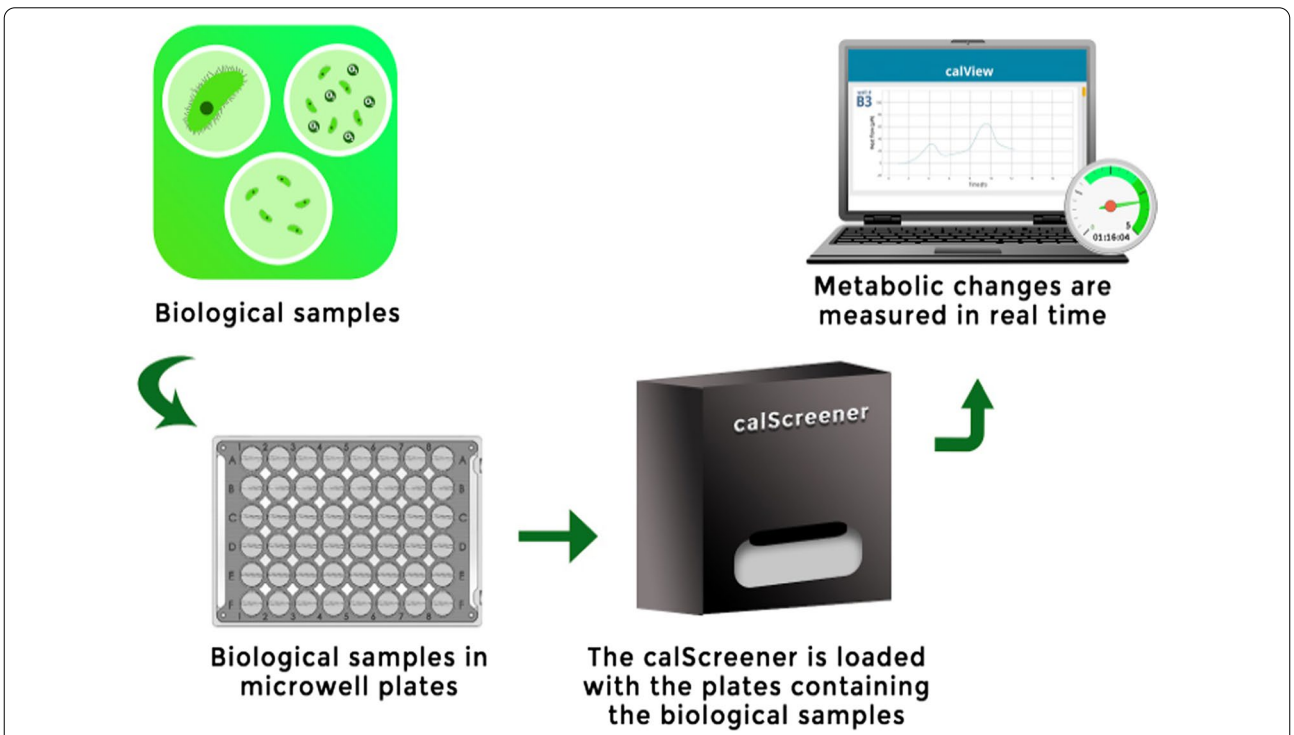

Fig. 1 Schematic framework of the isothermal microcalorimetry calscreener in metabolism measurement of biological specimens

that cell growth is associated with an enthalpy change, it is shown that the specific heat flow rate is stoichiometrically related to the net specific rates of substrates, products, and indeed to specific growth rate, and therefore a direct reflection of metabolic rate (Guan et al. 1998). All biological or non-biological chemical or physical processes either give off energy or absorb energy in the form of heat. The heat produced is as a result of oxidative breakdown of carbon source by the microbial population in the culture. Metabolically-active bacteria generate energy which is proportional to their growth rate in a given culture system (Tellapragada et al. 2020).

Isothermal calorimetry measures the heat flow of biological processes, which is directly related to the rate at which a given chemical or physical process progresses. The IMC calscreener machinery is concurrent with the categorization of thermodynamic features of macromolecules (Privalov and Dragan 2007), ligand-required interface (Russel et al. 2009), pathogen proliferation pattern and surveying of the inter-relational connection between biomolecules and whole cells (Braissant et al. 2013, 2015). It employs the working standard of gauging the metabolic heat discharge subtleties for observing bacterial systems thriving in aerobic, micro-aerobic and anaerobic settings (Wadseo et al. 2017). This modus operandi is conceptualized in the marginal heat production proportions in the array of little nanowatts and even to sub-nanowatt levels for calorimeters on a chip (Maskow et al. 2011). Consequently, this permits the observation of metabolic action of active cells in the order of 3000–30,000 active bacteria per millimeter.

Additionally, the IMC calscreener reads the overall energy as a consequence of altogether biotic, somatic and biochemical procedures and responses in a biological setup, indicating that the energy discharged by bacterial systems are proportionate to the overall metabolic responses (Robador et al. 2018). The heat levels in a microcalorimeter can be gauged in microwatt (μW) to read the metabolic kinematics of bacteria inside a closed scheme (Butini et al. 2019; Tellapragada et al. 2020). The high temperature (°C) discharged by bacteria is connected to their cellular utilities that highlight their metabolism and proportionate cellular biomass.

A case of in-vitro determination of minimum inhibitory concentration (MIC) of superbugs using isothermal microcalorimetry calscreener

When bacteria are exposed to antimicrobial agents, there is a direct impact on their metabolism, and as a result, the amount of energy released is altered. It is on the basis of this altered amount of energy released that IMC calscreener thrives, and allows for the detection of metabolism metrics and growth rate of superbugs after exposure to antimicrobial agents. Tellapragada et al. (2020) conducted an evaluation of an IMC calscreener to assay the MICs of 4 clinical isolates; *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* against some common antimicrobial agents. The bacterial strains were subjected to sensitivity testing using a list of commonly used antibiotics comprising amikacin, Ciprofloxacin, Cefotaxime, Meropenem, Colistin, Tazobactam, Sulbactam, Cefepime, Ceftazidime Piperacillin and Minocycline in varying concentrations.

Study outcome revealed that variations existed with the different antibiotics tested on the bacterial isolates concurrent with the time of experiment on the IMC system. Based on the characteristics of the test bacterial strains, there is a possibility for variation in the performance of a new susceptibility testing method (Matuschek et al. 2018). To ensure proper distribution of the test bacterial strains which were obtained from four different hospitals across Europe (Tellapragada et al. 2020), bearing in mind the proper cognizance of their MICs against common antimicrobial agents of medical importance, thus ensuring that the relationship between the IMC system and the standard MICs are established. This relationship in turn served as the basis to compare and properly evaluate the strength of the IMC system with the conventional susceptibility testing methods. The total rates of error recorded following the use of the IMC system was found to be between 1 and 3.7% amidst the four Gram-negative bacteria tested. Some of the inconsistencies observed can be elucidated by the difficulties of susceptibility testing reproducibility, which is common to all MIC methods. This is particularly seen in the interaction of colistin and *P. aeruginosa* as experimented by Tellapragada et al. (2020).

Due to the threat posed by multidrug resistance, a synergism of minocycline and sulbactam was recommended as treatment choice for the infections caused by *Acinetobacter baumannii*. Significant error was generated more often while trying to establish the MICs for minocycline and sulbactam, which has also been reported to be difficult when using other methods of susceptibility testing (Fernandez-Cuenca et al. 2017). It therefore became a necessity to further evaluate the IMC calscreener method for propensity to predict the MICs for the two antibiotics. A large pool of *A. Baumannii* strains which comprises of both the resistant phenotypes and the wild-type were used to arrive at logical inferences. In general, the relationship between the IMC methods with the reference method used presented an agreement which fluctuated between 90 to 100%, at 96.3% average. It is however important to say that the IMC method is a very sensitive testing approach, and like every other susceptibility testing methods, can generate inconsistent outcomes which

could arise as a consequence of error in pipetting or contaminations (Fernandez-Cuenca et al. 2017).

The study by Tellapragada et al. (2020) has revealed that the MICs of Gram-negative bacteria can be determined based on their metabolic activity by applying the IMC calscreener. It was also revealed that the IMC method generated faster results for MICs in some bacterial strains than the reference method. The IMC method also allowed the monitoring of the bacterial growth rates in real-time under the influence of respective antibiotics.

Pseudomonas aeruginosa is a Gram-negative organism common in the environment and clinical setting (Alabi et al. 2021). It is an important disease pathogen in humans particularly in infections that affect cystic fibrosis patients (Alabi et al. 2021). Infections with this pathogen portends serious problem mainly because of its natural and acquired resistance to antibiotics (Mielko et al. 2019). Additionally, its inclination to inhabit surfaces makes the cellular membranes numb to antimicrobials at curative dimensions (Wu and Li 2015), thereby making its biofilms measurement to ascertain the bacterium infectivity intensity paramount. The IMC calscreener is capable of measuring the energy released in an isothermal, closed system at microwatt levels and this property makes it a potential tool to study the growth kinetics of bacteria as demonstrated in the metabolism dimension of clinically-significant *P. aeruginosa* biofilms (Braissant et al. 2010; Butini et al. 2019).

Isothermal microcalorimetry calscreener in in-vivo and in-vitro antimicrobial therapy

There are automated methods that can be used for the detection of activity of antibiotics including determination of MIC (Felmingham and Brown 2001). The isothermal microcalorimetry calscreener (IMC) works real-time for the detection of the antimicrobial agents' activity by measuring the energy released by superbugs which would vary depending on the effect of antimicrobial agents. Furthermore, it can be used to determine the MIC of antimicrobial agents' in-vivo and in-vitro (von Ah et al. 2009) as well as evaluating the synergistic activity of two antibiotics (Tellapragada et al. 2020). von Ah et al. (2009) investigated the antimicrobial activity and determined the MIC of cefazolin, cefoxitin, ampicillin, piperacillin, aztreonam, amikacin, gentamicin, vancomycin, chloramphenicol, erythromycin, tetracycline and ciprofloxacin against *E. coli*, *Staphylococcus aureus*, *P. aeruginosa*, *Enterococcus faecalis* and *Streptococcus agalactiae* employing the IMC calscreener.

Tellapragada et al. (2020) evaluated the activity of an IMC method in the determination of the MIC of some multidrug resistant Gram-negative rods. *E. coli*, *K. pneumoniae*, *P. aeruginosa* and *A. baumannii* were tested and concluded that IMC calscreener was able to determine the MIC of the antibiotics; Amikacin (4e16 mg/L), Cefotaxime (0.12e4 mg/L), Ciprofloxacin (0.03e1 mg/L), Meropenem (0.06e16 mg/L) and Piperacillin/tazobactam (2e32 mg/L) against the pathogens studied. The use of IMC is greatly reproducible as proven by Tellapragada's study conducted in four European countries comprising Sweden, Spain, Italy and the Netherlands. Braissant et al. (2010) reported that the MIC values determined using microcalorimetry and that of Clinical Laboratory Standard Institute (CLSI) are analogous but the microcalorimetry has an edge as regards the activity of antibiotics at sub-inhibitory concentrations.

The susceptibility and MIC of *Mycobacterium* sp to amikacin, clarithromycin, linezolid and ciprofloxacin was evaluated using IMC (Boillat-Blanco et al. 2015). von Ah et al. (2018) also determined the susceptibility of mixed bacterial culture to antibiotics as well as the MIC. Additionally, IMC has been used to determine the susceptibility of yeasts to antimicrobials (Astasov-Frauenhoffer et al. 2020) which supports the claims that IMC (Isothermal microcalorimetry calscreener) have been used not only in in-vitro analysis but also in in-vivo studies. In the determination of synergism between two antibiotics, Kasper et al. (2021) investigated the effectiveness of Meropenem when combined with colistin, rifampicin and amikacin against *E. coli*, *K. pneumoniae*, *P. aeruginosa*, and *A. baumanii* by measuring the metabolic activity. The result of the study suggested a prediction of an additive and synergistic drug combination for the treatment of multidrug resistant infection based on the metabolic readout. Wang et al. (2019) also investigated the synergistic activity of three antibiotics; fosfomycin, ciprofloxacin and gentamicin against *E. coli* and *P. aeruginosa* from patients with prosthetic joint associated infection and their anti-biofilm activity using the IMC calscreener.

Biofilm formation in bacteria and isothermal micro-calorimetry calscreener

Butini et al. (2018a, b) analyzed the activity of frequently set antimicrobial agent on two laboratory strains of *S. aureus* executed by IMC. Study demonstrated that both planktonic-entrenched methicillin-resistant and methycillin-susceptible *S. aureus* were liable to glycopeptide antimicrobials employed (EUCAST 2017), whereby an appreciably elevated proportions of anti-staphylococcal drugs were required to exterminate the biofilm of the *S. aureus* species. *Staphylococcus aureus* biofilm constitute a key role in metal implant-causing maladies. The mounting usage in metal implants fosters the advancement of infections intricated to manage due to *S. aureus* forming biofilm on in-dwelling metallic surface thereby eliciting potential risk of *Staphylococcus aureus*-caused infections

in the human body (Butini et al. 2018a, b). Contemporary curative preferences comprise antimicrobials with inhibitory bactericidal and bacteriostatic tendencies both as solo and synergistic regimens adopting mainly glycopeptides; vancomycin, daptomycin, rifampicin and fosfomycin as treatment modes (Butini et al. 2018a, b). Vancomycin is a chief pharmaceutical alternative for the preventing and treating of enveloping staphylococcal infections (Liu et al. 2011), though, the glycopeptide elicit a measured bactericidal action on Gram-positive bacteria (Ghareeb et al. 2021).

Staphylococcus aureus is a pathogenic organism accountable for an extensive assortment of bacterial infections with human anatomic bearings comprising bloodstream, respiratory tract, skin, and bone (Kuroda et al. 2001; Tong et al. 2015). *Staphylococcus aureus* as well inhabits the tissues of the necrosis and non-living surfaces, thereby forming biofilms (Arciola et al. 2015). Inside a biofilm, a bacterium is entrenched in an extracellular milieu, building up into a multifaceted bacterial enclave presenting serviceable and structural diversity (Zimmerli et al. 2004).

For in-vivo studies, the biofilm extracellular milieu might shield the entrenched bacterial cells from the assault of some chemotherapeutic agents and host immune framework (Bjarnsholt et al. 2013). Biofilms are also exemplified by cells with a dawdling and non-growing physical characteristic, which are able to adapt in conjunction with elevated portions of bactericidal antimicrobials (Lewis 2005), consequently eliciting disease reoccurrence. A good epitome of persister cells in *S. aureus* symbolizes a diminutive proportion of a microbial population, which are hereditarily prone with phenotypic recalcitrance to chemotherapeutic agents owing to their non-growing inert state (Fisher et al. 2017; Grassi et al. 2017). Persistence is, hence, strikingly dissimilar from resistance, which is an innate ability attained by the entirety of the microbial population and it denotes the tendency of bacteria to proliferate in tandem with soaring proportions of antibiotics with non-dependence on the infection management interval (Scholar and Pratt 2000; Brauner et al. 2016).

The purpose of antimicrobial vulnerability is of elemental significance throughout the advanced modus operandi of novel antimicrobial drugs´ discovery, and in forecasting probable restorative upshot during the chemotherapeutic cure of an infection. About 80% of human infections are due to immobile bacteria, the adoption of biofilm-explicit antimicrobial assay is desirable (Percival et al. 2015; Ciofu et al. 2017). This elicited the idea of the isothermal microcalorimetry calscreener (IMC) which is an extremely responsive procedure that facilitate an instantaneous screening of bacterial practicability in terms of metabolism-associated heat fabrication (Braissant et al. 2010). This scheme is an extensively used and validated for testing the anti-biofilm action of diverse antimicrobial combinations, comprising antibacterial agents (Oliva et al. 2014; Butini et al. 2018a, 2018b; Casadidio et al. 2018), antifungals (Furustrand et al. 2013) and bacteria-eaters (Tkhilaishvili et al. 2018a, 2018b).

Application of the IMC for establishing the microbial activities of clinical and ecological bacteria

Isothermal micro-calorimetry calscreener (IMC) has been utilized in a variety of microbiological fields. The possibilities are demonstrated through medical and environmental applications (Table 1). It is a widely used technique for determining the amount of energy emitted during metabolic activities in a biological system. In addition, when it comes to investigating AST, IMC provides various advantages over standard test methodologies (Tellapragada et al. 2020). IMC is particularly useful in environmental microbiology for measuring bacterial activity without the need to culture species separately or add radio-labeled, fluorescent, or chromogenic substrates. As a result, IMC is a great supplement to molecular research. Many different processes have been investigated using IMC.

Rong et al. (2007) identified three broad types of soil-related IMC research. These are: (1) microbial activity detection and quantification, (2) organic pollutant toxicity and degradation monitoring, and (3) risk assessment linked with heavy metal (and metalloid) pollution (Braissant et al. 2010) (Table 1). It was discovered that viable cell counts of bacteria and fungi were significantly connected to IMC-measured heat generation as regards detecting and quantifying microbial activity (Russel et al. 2009).

In medical microbiology, early and correct identification of infectious disease is vital because proper diagnosis can increase the effectiveness of treatments and help the infected patient avoid long-term problems (Braissant et al. 2010). Rapid isothermal micro-calorimetric detection of bacterial infection or contamination is one notable medical application, which is crucial in promptly executing the appropriate treatment (Braissant et al. 2010). IMC can detect bacterial contamination of donated blood platelets in as short as a few hours, according to recent research. IMC can be used to determine MICs in Gram-negative bacteria that are extensively drug-resistant as juxtaposed by Butini et al. (2019).

Isothermal microcalorimetry calscreener (IMC): case of the relationship between mineral-influenced microbial population in bioleaching and microbially-induced corrosion (MIC)

Didi et al. (2017) reported that bioleaching operations, microbial colonization of mineral ore is crucial for

Table 1 Peculiarities of the isothermal microcalorimetry calscreener (IMC) in medical microbiology applications

Microbiological application	Specificity of application	References
Medical microbiological application	The detection of bacterial contamination in donated blood platelets	Trampuz et al. (2007)
	The determination of inhibitory effects for diverse antimicrobial compounds and microorganisms	Xi et al. (2002), Yang et al. (2008) and von Ah et al. (2009)
	The determination of heat flow in the growth pattern medically-relevant bacteria	Von Ah et al. (2008) and Baldoni et al. (2009)
	Distinguishing the growth rates of methycillin-susceptible *Staphylocococcus aureus* from methycillin-resistant *Staphylococcus aures*	von Ah et al. (2008) and Baldoni et al. (2009)
	The measurement of the growth and heat of adsorption in mouth bacteria (halophilic bacteria) on surfaces in dentistry	Hauser-Gerspach et al. (2008)
	The examination of viral maladies and antiviral compounds activity via high heat emission from infected cells in contrast to the uninfected control cells	Tan and Lu (1999) and Heng et al. (2005)
Environmental microbiological application	The assessment of ecological bacterial activities in lake and marine sediments via heat production	Pamatmat and Bhagwat (1973) and Pamatmat et al. (1981)
	The measurement of the heat production of lake sediments comprising mixed cohorts of anaerobes, fermenters and aerobes	Haglund et al. (2003)
	The observational studies on the relational dynamics of heat production on adenosine triphosphate (ATP) and dehydrogenases assay (triphenyltetrazolium and iodonitrotetrazolium chloride) in *Caenorhabditis elegans*	Braeckman et al. (2002)
	The measurement of the heat production of aquatic protists in ascertaining the allometric relativity, amidst mass, surface area, and metabolic rate	Johnson et al. (2009)
	The investigation of the microbial population, organic organic acid contaminant/toxicity and heavy metal contamination by heat production in soil microbiology	Rong et al. (2007) and Critter et al. (2002)
	The assessment of soil composting processes	Laor et al. (2004)

successful mineral solubilisation and metal recovery. An improved comprehension of the mechanisms and behaviours by which microorganisms cling to and colonize mineral surfaces could aid bioleaching (Didi et al. 2017). Direct measurement of metabolic activity of mineral-related cells is difficult and has not been proved effectively in heap leaching ore beds. The metabolic activity of a mixed mesophilic culture colonizing the mineral surface was measured using the isothermal microcalorimetry (IMC) calscreener as demonstrated by Didi et al. (2017). As a rider to this, Abbass and co-workers' study on weight loss, electrochemistry, and scanning electron microscopy (SEM) investigations of 1-butylpyrrolidinium chloride ionic liquid as an environmentally-friendly rust inhibitor for oilfield equipment (Abbas et al. 2019) could aid in the utilization of the IMC in electrochemistry for the control of microbially-induced corrosion of oil pipes via the metabolism depth and possibly for metal recovery. El-Shamy and co-workers' report on the control of corrosion and microbial corrosion of steel pipelines in salty milieu by polyacrylamide (El-Shamy et al. 2016) also represent a promising approach that can be applied incorporating the IMC calscreener for metal recovery as similarly demonstrated by Didi et al. (2017). El-Shamy and Bar's work on the peculiarity of ionic liquid as water solvable and budding inhibitor in microbial corrosion, and for iron artifacts (El-Shamy and Bar 2021) also highlights the possible application of environmentally-harmless chemicals and the IMC calscreener by metabolic activity measurement. Additionally, Shehata and associates' observations from the antibacterial impact of two ionic liquids (1-(2-hydroxyethyl)-3-methylimidazolinium chloride and 1-ethyl-3-methyleimidazolinium chloride) and their corrosion inhibition output (Shehata et al. 2020) also buttress the possibility of the IMC calscreener in the metal preservation and recovery using ionic liquid chemicals. Moreso, El-Shamy's review on the biological-killing effect of some chemical structures on the sulphate-reducing bacteria (SRB) and nitrate-reducing bacteria (NRB) responsible for microbial corrosion

(El-Shamy 2020) also strengthens the hypothesis for the application of the IMC calscreener in metal recovery of oil and gas pipelines. The antibacterial and anti-corrosion properties of Trifluoromethylsulfonate of 1-butyl-1-methylpyrrolidinium for the effectual inhibition of the planktonic and stalkless bacterial growth with strong efficiency as reported by El-Shamy et al. (2015) also aided the possibilities of employing the metabolic kinematic dynamics of the IMC calscreener in metallic compounds recovery. El-Shamy's research outcome on the utilization of cinnamaldehyde at room temperature and pressure on carbon steel in 3.5% saline condition (El-Shamy et al. 2020) could further emphasize the probable utilization of the IMC calscreener for corrosion inhibition of metal surfaces.

Conclusions

Isothermal microcalorimetry (IMC) calscreener has become a more prominent tool in in-vivo and in-vitro antimicrobial therapy. It is based on the principle of measuring energy from cell metabolism and hence has high sensitivity in measuring early detection of resistance/inhibition of multidrug resistance bacteria. The energy released in an isothermal, closed system at microwatt levels makes the IMC a potential tool to study the growth kinetics of bacteria in real-time under the influence of respective antibiotics. It is also extensively used and validated for testing the anti-biofilm action of diverse antimicrobial combinations, comprising antibacterial agents. Isothermal micro-calorimetry (IMC) calscreener should be more preferred in accessing the automated peculiarities of in-vivo and in-vitro antimicrobial therapy and metabolism measurement of multidrug resistant bacteria with possible applications in metal recovery.

Abbreviations

DDT: Disc diffusion test; BMD: Broth micro-dilution; MIC: Minimum inhibitory concentration; MDR: Multidrug resistant; IMC: Isothermal microcalorimetry calscreener; CLSI: Clinical Laboratory Standard Institute; EUCAST: European committee on antimicrobial susceptibility testing; AST: Antibiotic susceptibility test; SEM: Scanning electron microscopy; SRB: Sulphate-reducing bacteria; NRB: Nitrate-reducing bacteria.

Acknowledgements

The authors recognize the scholars whose literature studies have been cited to write this review article.

Author contributions

MTB designed the concept of the review and drafted the model. MAA, OJB, MES, BTL, AFO performed the literature survey and formatting. MOE and DIL performed a plagiarism check and structure the review. MAA proofread the manuscript. All authors read and approved the final manuscript draft.

Funding

None was received.

Availability of data and materials

Not applicable.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Received: 22 April 2022 Accepted: 15 May 2022
Published online: 23 May 2022

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