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মহাভারত ও সাংখ্যকারিকার নিরিখে প্রকৃতি – একটি সমীক্ষা

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Abstract:
The Mahābhārata is one of those Smṛti texts that have a lot of material on Indian śāstras along with which is morals and teachings associated with the Indian schools of philosophy. Throughout the vast expanse of the text Vedānta and other schools of philosophy are represented but arguably the most importance has been accorded to the Sāṃkhya system. Of the 25 Sāṃkhya tattvas the prakṛtitattva has featured prominently in the Mahābhārata and has gotten treatment which is unique to the grand epic. The prakṛtitattva has received its proper and elaborate treatment in Īśvarakṛśṇa's Sāṃkhyakārika and this opens the arena for a comparative analysis of the tattva in terms of their treatment in the Mahābhārata and the Sāṃkhyakārika. What emerges is that the principle has been handled almost similarly except for the introduction of the concept of Īśvara in the Mahābhārata which sits atop prakṛti and controls its actions, while in the Sāṃkhyakārika it is completely independent.

Keywords: Mahābhārata, Sāṃkhyakārika, prakṛti, avyakta, guṇa

মহাভারত ভারত-ইতিহাসের পুর্ণাঙ্গ দলিল। মহাভারতের সমগ্র সাহিত্য কাঠামোয় প্রলিপ্ত হয়ে আছে ভারত সভ্যতার সর্বাঙ্গীন ইতিহাস। আলংকারিক বিচারে মহাভারত মহাকাব্যের সংজ্ঞায় বিভূষিত হলেও মূলত এটি একটি সংকলন গ্রন্থ। ভারতীয় বিদ্যার এমন কোন ক্ষেত্র নেই যা মহাভারতের দ্বারা স্পৃষ্ট হয়নি। তাই মহাভারতের মহাত্ম্য কীর্তন করতে গিয়ে নির্দিদ্ধায় উচ্চারিত হয় – যন্নেহাস্তি ন তৎ ক্বচিৎ। অর্থাৎ যা নাই ভারতে তা নাই ভারতে। মহাভারতকে আমরা যেভাবেই অন্বেষণ করি সে সেইভাবেই ধরা দেয়। একথা বললে অত্যুক্তি হবে না যে মহাভারত হল একই আধারে ভারতীয় সভ্যতা সংস্কৃতির সর্বাঙ্গীন ইতিহাস, সম্পূর্ণ সাহিত্য, সামগ্রিক সমাজবিদ্যা ও পরিপূর্ণ নীতিবিদ্যা ও পূর্ণ দর্শন।

আঠারোটি পর্বের সমন্বয়ে গঠিত বিপুলাকার শরীরে মহাভারত অন্যান্য বিবিধ বিষয়ের ন্যায় ভারতীয় দর্শন চিন্তাকেও ধারণ করেছে ও তাকে বহন করে নিয়ে চলেছে। মহাভারতের সমগ্র আয়তনের বিভিন্ন অংশে যে দর্শনভাবনাগুলি প্রস্ফুটিত হয়েছে তাদের পুঙ্খানুপুঙ্খ বিশ্লেষণ করলে সুস্পষ্টভাবে বোঝা যায় যে এগুলি সবই ছয়টি আস্তিক দর্শনের কোন না কোন নীতির চিন্তাপ্রসূত। অর্থাৎ মহাভারতের সমগ্র দর্শনচিন্তা প্রকৃতপক্ষে ভারতীয় ষড়দর্শনেরই চিন্তা। এই ছয়টি দর্শনের মধ্যে আবার বিশেষ মাত্রায় প্রাধান্য পেয়েছে

সাত্ত্বিকভাবের কার্য, যা নিজের দুঃখযুক্ত ও অপ্রীতিকর হয় তা রজোগুণের কার্য এবং যা দেহ ও মনকে মোহমুক্ত করে এবং তাতে অনির্বচনীয় ও অজ্ঞেয় ভাব সঞ্জাত করে তা তমোগুণের কার্য –

অত্র যৎ প্রীতিসংযুক্তং কায়ে মনসি বা ভবেৎ।
বর্ত্ততে সাত্ত্বিকো ভাব ইত্যুপেক্ষেত তত্তথা।।
অথ যদ্দুঃখসংযুক্তমপ্রীতিকরমাত্মনঃ।
প্রবৃত্তং রজ ইত্যেব তদসংরভ্য চিন্তয়েৎ।।
অথ যন্মোহসংযুক্তং কায়ে মনসি বা ভবেৎ।
অপ্রতর্ক্যমবিজ্ঞেয়ং তমস্তদুপধারয়েৎ।।[19]

গুণসমূহের কার্য বিষয়ে নীলকণ্ঠের ভারতভাবদীপ টীকার বক্তব্যটিও বিশেষভাবে লক্ষ্যণীয়। সেখানে বলা হয়েছে সত্ত্বগুণ হতে দয়া প্রভৃতি, রজো থেকে আসক্তি বা কাম প্রভৃতি এবং তমো গুণ থেকে মোহ প্রভৃতি ধর্ম উৎপন্ন হয়ে থাকে – 'সত্ত্বস্য গুণাম্ ধর্ম্মাদীন্ রজসঃ প্রবৃত্ত্যাদীন্ তমসোঽপ্রবৃত্যাদীন্...'।[20]

কোনো কার্য সাধনের ক্ষেত্রে সত্ত্বাদি গুণত্রয় যেরূপ ভূমিকা পালন করে থাকে তার উপর ভিত্তি করে সাংখ্যশাস্ত্রে গুণগুলির চরিত্র নিরূপণ করা হয়েছে। এবিষয়ে ঈশ্বরকৃষ্ণ সাংখ্যকারিকায় বলেছেন সত্ত্বগুণ হল লঘু ও প্রকাশক, রজোগুণ প্রবৃত্তিশীল ও চঞ্চল অর্থাৎ ক্রিয়াশীল এবং তমোগুণ গুরু ও আবরণক –

সত্ত্বং লঘু প্রকাশকমিষ্টমুপষ্টম্ভকং চলং চ রজঃ।
গুরু বরণকমেবতমঃ ...।।[21]

সাংখ্যকারিকার এই বক্তব্যের সমর্থন মেলে নীলকণ্ঠের টীকায় – 'তামসান্ ক্রোধাদীন্, রাজসান্ প্রবৃত্ত্যাদীন্, সাত্ত্বিকান্ প্রকাশাদীন্'[22]। তাছাড়াও নীলকণ্ঠ ভারতভাবদীপে সত্ত্ব, রজো ও তমো গুণের শুক্ল, লোহিত ও কৃষ্ণবর্ণ ধারণের হেতুরূপে স্বচ্ছত্ব, রঞ্জকত্ব ও মলিনত্বকে উল্লেখ করেছেন যা পক্ষান্তরে সত্ত্বাদি গুণের যথাক্রমে প্রকাশত্ব, ক্রীয়াশীলত্ব ও আবরকত্ব ধর্মকেই নির্দেশ করে – 'ক্রমেণ স্বচ্ছত্বাদ্রঞ্জকত্বান্মলিন্ত্বাচ্চ সত্ত্বাদীনি শুক্ললোহিতকৃষ্ণানি...'[23]। অতএব উপরোক্ত আলোচনার ভিত্তিতে বলা যায় যে গুণের স্বরূপ, ধর্ম ও কার্য বিষয়ক বক্তব্যে মহাভারত ও সাংখ্যকারিকার মধ্যে কোন বৈসাদৃশ্য নেই।

ত্রিগুণাত্মিকা এই প্রকৃতি তত্ত্বই যে অব্যক্ত তত্ত্ব একথা প্রকৃতির পর্যায়শব্দ আলোচনার প্রসঙ্গে পূর্বেই বলা হয়েছে। ব্যক্ত তত্ত্ব হল প্রকৃতি ও পুরুষ ব্যতীত মহদাদি তেইশটি বিকারযুক্ত পদার্থ – 'তত্র ব্যক্তলক্ষণমাহ প্রোক্তমিতি। তচ্চ মহদাদি বিকারান্তং ত্রয়োবিংশকম্'[24]। মহাভারতে বলা হয়েছে অব্যক্ততত্ত্বের স্বরূপ অবগত হওয়ার পূর্বে ব্যক্ততত্ত্বকে জানা প্রয়োজন কারণ তাতে অব্যক্ত সহজবোধ্য হয়ে ওঠে –

'তত্রাব্যক্তময়ী বিদ্যাং শৃণু ত্বং বিস্তরেণ মে।
তথা ব্যক্তময়ঞ্চৈব সাংখ্যে পূর্ব্বং নিবোধ মে।।[25]

ব্যক্তের যা ধর্ম অব্যক্ত তার বিপরীত ধর্মবিশিষ্ট। ব্যক্তের ধর্ম নির্দেশ করে মহাভারতে বলা হয়েছে ব্যক্ত হল জন্ম, বৃদ্ধি, জরা ও মরণ এই চারটি লক্ষণযুক্ত –

প্রোক্তং তদব্যক্তমিত্যেব জায়তে বর্দ্ধতে চ যৎ।
জীর্য্যতে ম্রিয়তে চৈব চতুর্ভিলক্ষণৈর্যুতম্।।[26]

[29] সাংখ্যকারিকা - ১০, পৃ ১১৭

[30] তত্ত্বকৌমুদী, সাংখ্যকারিকা - ১১, পৃ. ১২৭

[31] মহাভারত, ১২.৩০২.১২, পৃ. ১৬৭২ (পুণা সংস্করণ)

[32] মহাভারত ১২.৩০২.১৩, পৃ. ১৬৭২ (পুণা সংস্করণ)

[33] গৌড়পাদভাষ্য, সাংখ্যকারিকা - ১০, পৃ. ৪৯-৫০

[34] মহাভারত, ১২.২৯৪.৩৩, পৃ. ১৬৩৫ (পুণা সংস্করণ)

[35] সাংখ্যকারিকা - ২১, পৃ. ১৯৭

[36] ভগবদ্গীতা ১৩.২৬, পৃ. ৪২৩

[37] ভগবদ্গীতা ৯.৭-৮, পৃ. ৩১৪

[38] ভারতকৌমুদী, মহাভারত, ১২.২৯৯.২২, পৃ. ৩১৬৯

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Content

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ASCERTAINING THE MEANING OF SĀṂKHYA

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Abstract

Naming of any idea or material is extremely important as it provides one with a general introduction and basic or initial conception of the idea under discussion. Amongst the *Ṣaḍadarśana*, except for the case of Sāṃkhya, a very definite connection to a particular root-word and their nomenclature can be established. For example, the term '*vedānta*' refers to the end or termination point or the ultimate philosophical maxims of the Veda as encapsulated in the phrases *brahmavidyā* or *ātmajñāna*. Therefore, there is no confusion regarding the naming of the Vedānta school of philosophy. Etymologically *sāṃkhya* means *samyaka jñāna* or complete knowledge. But, at different times and in different texts such as the *Mahābhārata* and *Arthaśāstra* terms such as *anvīkṣā*, *parisaṃkhyāna* provides it with differing interpretations. Therefore, the emergence and the naming of Sāṃkhya as a philosophy that expounds the *tattva*s related to the interplay of *prakṛti-puruṣa* gives rise to a host of questions. And these can only be answered by complete explanation of the term *sāṃkhya*.

Key Words: *Sāṃkhya*, *saṃkhyā*, *parisaṃkhyāna*, *samyaka jñāna*, *anvīkṣā*, *Mahābhārata*, *Arthaśāstra*

Of the six systems of Indian philosophy Sāṃkhya is one which is very well-known, acclaimed as being ancient and has been well-analysed. Studies of its antiquity were very common in the 19th century and were noted as such even by the German scholar Garbe. Larson quoting him says that, 'there can be no doubt.... that Sāṃkhya is one of the oldest philosophies of the Indian tradition.'[i] In the *Śāntiparva* of the Mahābhārata the importance and depth is enthusiastically proclaimed by the authors when they record the following – *nāsti sāṃkhyasamaṃ jñānaṃ*.[ii] Similarly, the *Śvetāśvatara Upaniṣad* states – '*tatkāraṇaṃ sāṃkhya-yogādhigamyam*'[iii] – meaning that the Universal Cause can only be accessed by *Sāṃkhya-yoga*. In many of the *Smṛtis* the term '*sāṃkhya*' was used various times as a synonym for *jñāna*. For example, in the *Bhagavata Gītā jñāna-yoga* is referred to as *jñānayogena sāṃkhyanām*[iv] or as '*yat sāṃkhyaih prāpyate sthānam*'[v] *Sāṃkhya* is also affirmed as '*kṛtānta*', – *sāṃkhye kṛtānte proktāni siddhaye sarbakarmaṇām*[vi] – its acclamation as the pathway to inference of the *ātman*. The above-mentioned laudatory examples from an eminent text such as the *Bhagavata Gītā* show the high prestige it had amongst the *brāhmaṇa*s. The adulation provided by the *Gītā* shows the importance that was accorded to the Sāṃkhya system of knowledge,

It would be prudent at this moment in this paper to define the meaning of the term *sāṃkhya*, a very difficult task when put in contrast to defining the other members of the Ṣaḍadarśana such as Vedānta, Mīmāṃsā, Nyāya etc. These terms come with their meaning laden in them, not something that can be said for *sāṃkhya*. The definition provided by the dictionaries for the latter does not indicate any specific system or school of philosophy and therefore the basics of the philosophy that the appellation indicates are not found easily. And hence the need for explicating the term becomes essential. In this paper my attempt would be to explain the definition(s) of Sāṃkhya, specific to the contexts, to find the reasons for the establishment of the term as a system of philosophy that originated in the works of *Maharṣi* Kapila.

The affixation of 'sam' with the 'khyā' root gives the word 'saṃkhyā'. 'Saṃkhyā' in common parlance translates as numbers, 1, 2, 3, etc.[vii]. It is from this word the term Sāṃkhya emerges. Hence the

complete vision which can be understood as complete philosophy which results in the complete knowledge or *satya jñāna*. The knowledge that helps in the discernment of perpetual, predictable and therefore inanimate and passive matter or *jaḍaprapañca* from *puruṣa* who is continually changing and animation itself is *satya jñāna*. This has moreover, been termed as *vyaktāvyakta-vijñāna*, *vivekakhyāti*, *viveka-jñāna* etc. *Saṃkhyā samyagvivekenātmakathanamityarthah* – this quotation by Vijñānabhikṣu in *Sāṃkhyapravacana-bhāṣya* makes it crystal clear that the word *saṃkhyā* here is used in its epistemological sense. And, moreover, he had no intention of using the word in its numerological denotation.

sāṃkhyadarśanametāvatparisaṃkhyānadarśanam

sāṃkhyam prakurute caiba prakṛtim ca pracakṣate[xviii]

tattvāni ca caturviṃśat parisaṃkhāya tattvatah

sāṃkhyāh saha prakṛtyā tu nistattvah pañcaviṁśakah[xix]

A different reading of the last referred *śloka* of the Mahābhārata can be found in *Pravacana- bhāṣya* by Vijñānabhikṣu where he writes –

saṃkhyām prakurvate caiba prakṛtim ca pracakṣate

tattvāni ca caturviṃśat tena sāṃkhyām prakīrtitā[xx]

The word '*saṃkhyā*' is used here as referring to the acquirement and analysis of self by way of complete *viveka*. Hence, there can be no doubt regarding its use and understanding by Vijñānabhikṣu. The mere numerological connotation of the term is not acceptable to him as exemplified here.

Several other scholars have followed Vijñānabhikṣu's interpretation of the term *saṃkhyā* as given in the Mahābhārata. They are also of the opinion that the use of term in Mahābhārata is primarily epistemological. This is based on the idea that the Mahābhārata talks of *paramapuruṣa*'s aim of achieving *mokṣa* or *kaivalya* as being attained by knowledge about the *vivekajñāna* of *prakṛti* and *puruṣa*. Since the Sāṃkhya philosophy as elucidated here is based completely on the idea of *vivekajñāna* and its achievement it would foolish to suggest any other usage or utilisation than epistemological. Even the synonymical *saṃkhyān* is used in the sense of theory of knowledge. For example, the Bhagavadagītā says – *procyante guṇasaṃkhyāne*[xxi]. Similar application can be viewed in the Bhāgavata Mahāpurāṇa when it states '*namo bhagavate mahāpuruṣāya sarvaguṇasaṃkhyānāyānantāyāvyaktāya nama iti*'.[xxii] This is made manifest in Śrīdhara's commentary when he notes - *sarveṣāṃ guṇānāṃ saṃkhyānāṃ prakaśo yasmāt*.[xxiii] He is explicit of the root of '*saṃkhyā*' being '*sāṃkhya*', the latter meaning comprehensive knowledge or *samyaka jñāna*, and Sāṃkhya Śāstra is the repository wherein it resides.[xxiv] Even the Mahābhārata supports this when it says - *sāṃkhyajñānaṃ pravakṣyāmi parisaṃkhyānadarṣanam*.[xxv]

However, it should be mentioned that though the epistemological interpretation of the term *saṃkhyā* as explained by the attainment of comprehensive knowledge of *viveka* by understanding the nature of the relation between *prakṛti- puruṣa* has been given primacy the numerological explanation of it should not be ignored at all. Many scholars, both from, Orient and Occident have given special attention to such an explanation.

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POEMS

Holocaust Consciousness in V.S. Naipaul's *In a Free State* - A Different Perspective

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Abstract

The paper attempts to show why in the postcolonial world the term 'Holocaust' can never be considered as a specific historical phenomenon; rather it must be used in its wider implication as the world we inhabit is full of human suffering in view of the painful plights of displaced communities worldwide. Besides bringing out V.S.Naipaul's Holocaust consciousness manifested in his portrayal of unhappy lives of displaced people, lives pathetically 'free' from any sense of belongingness, their challenges and predicaments in the context of In a Free State*, the author tries to justify the use of 'comic' in Holocaust comedies keeping in view Naipaul's unique use of 'comic.'. Moreover by finding parallelisms from Holocaust film comedies Naipaul's use of 'comic' is considered. The paper tries to theorize the need of taking resort to 'comedy' in order to survive in a world full of threats and challenges.*
Keywords: Displacement, Holocaust, comic, Parallelisms

> "It's amazing. The race that has suffered the most is obviously the Jews in the Holocaust, and the Jewish humour is very much a part of suffering."
>
> Walcott and Baer 1996, 171

> "I took refuge in humour – comedy, funniness, the satirical reflex, in writing as in life, so often a covering up for confusion".
>
> *The Enigma of Arrival* 1987, 167

Introduction

Comedy for ages has remained a matter of controversy in literature. The arguments traditionally placed against comedy are: "Addressing motifs of ridicule, comedy is itself ridiculous and can, thus not be taken seriously. It cannot prove a source of insight as tragedy can" (Dadlez and Luthi 2018:81). Tragedy is viewed as the highest kind of literary form whilst comedy is held inferior to it. As says Stolnitz, comedy is "lower than tragedy not only because of the lesser intensity, complexity and subtlety of our response…but also because it lacks the compactness and vividness of structure which, as tragedy unfolds in time, creates a tightly-knit, climactic and integrated experience in the spectator" (Stolintz 1955:60). However, the similarities between tragedy and comedy have been underlined by a number of

and Linda to get from their lives in the land of their self-chosen exile. Bobby is tortured at the barrack room by the army and it sends an echo back to the persecution of man in the regime of Nazi Germany. In the "Epilogue" we are once more disturbed when Naipaul shows how the whipping of the Egyptian beggar boys can be entertaining to the travelers and the book ends with reference to the "ragged waiters" (Naipaul, 246), "agitated peasant crowds" and "defeated soldiers" who are to know total defeat in the desert" (Naipaul, 247). Thus, throughout the book Naipaul's focus is on helplessness, suffering and victimization of poor mankind. Holocaust never needs to be mentioned. But its absence never lets one forget the "presence" of it as the torture and persecution of mankind and the resultant pain and suffering of poor human folk is as present as ever. Only the machinery of torture gets changed in ages. However, not only thematically but also in his use of 'comic' Naipaul's novella has resemblances with that of a Holocaust film comedy.

A Holocaust comedy does not end happily. Similarly, here neither of the stories has happy ending. The marriages that take place in the first two stories are not indicative of better future. Naipaul uses humour mostly to show the wrongness of the situations. For instance, sometimes we are tempted to view Santosh as a comic character. At times his situations appear to us funny. But beneath that what is apparently amusing, there lies the central sadness of his position. The very first day Santosh comes to Washington, he starts feeling completely "enclosed" Santosh's discomfort at the sound of air-conditioner or the sense of enclosure of a man who has never been in an aeroplane before or has never used an elevator is comic. But the suggestions of an incremental enclosure serve to underline the systematic reduction of freedom attending the life of a migrant. It seems that in Holocaust comedy when no more laughter is possible, the hero tends to achieve a tragic dignity; he becomes almost a heroic figure. It applies to Naipaul's second story which is almost devoid of the comic touches. One major function of humour is that it helps one to go through the trauma of living. But in this story the narrator is to suffer so terribly, that he fails to retain his sense of humour. It further causes a severe nervous breakdown and though he recovers from it, he ultimately becomes a pathetic figure. But he is still heroic in the sense that he is not a completely defeated character. He thinks of sending a message of death to his home but he does not commit suicide even in the face of utter hopelessness. In the final story Linda is allowed to employ her sense of humour to go through her sense of trauma. But finally it is the horrible situation all around her that makes her sense of humour stop working. In the final story once again there are some sources that give rise to comic pleasure as the characters here attempt to have comic escape. It is true that the situation is so horrible that they are not allowed such escapes but their attempts to take resort to humour to go through the trauma of living almost symbolizes Naipaul's attempt to represent the horror of living comically. However, it is to be noted that the principal feature of a Holocaust film comedy is to present horror comically. The task is a difficult one as at the same time it should not appear as a comic entertainment. Though Naipaul uses 'comic', the novella cannot be called a comedy. The book is even not a tragedy as no great tragedy befalls any of these characters. Zizek (Zizek 2000:26-29) discusses the failure of tragedy and comedy genres to represent the Holocaust. Naipaul writes here from the deepest ironic vision, in the words of Friedlander the "tragic-ironic" vision (Friedlander 1988:289), the same that permeates a Holocaust comedy.

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এবং মহুয়া

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সম্পাদক

ড. [illegible]

কে.কে. প্রকাশন

গোলকুঁয়াচক, মেদিনীপুর, প.বঙ্গ।

বাংলার নবজাগরণের প্রাণপুরুষ
রাজা রামমোহন রায় ও বর্তমান সমাজ

সরোজ কুমার সরকার

সার সংক্ষেপ :

আগামী বছর ২০২২ সাল রাজা রামমোহন রায়ের ২৫০ তম জন্মবার্ষিকী। ভারতের প্রধানমন্ত্রী শ্রী নরেন্দ্র মোদী ঘোষণা করেছেন ২৫০তম জন্মজয়ন্তী সারা ভারতে পালন করা হবে, রামমোহনের ভাবনা ও কর্মধারার মূল্যায়ণে। তাঁর মৃত্যুর প্রায় দ্বিশত বৎসর পরেও তিনি আমাদের সামাজিক, রাজনৈতিক অর্থনৈতিক জীবনে, চিন্তা চেতনা ও মানবিকতার ক্ষেত্রে কতটা প্রাসঙ্গিক তা এই প্রবন্ধে ব্যক্ত করার ক্ষুদ্র প্রয়াস মাত্র। তিনি বাংলার নবজাগরণের প্রাণপুরুষ। মহৎ সমাজ সংস্কার, বহু ভাষাবিদ, শিক্ষাবিদ, ভারতের প্রথম নারীবাদী ও একজন মানবতাবাদী।

প্রতিপাদ্যবিষয় :

রাজা রামমোহন রায় বাংলার নবজাগরণের পথিকৃৎ। ইউরোপের নবজাগরণের ক্ষেত্রে সেই দেশের শিল্প, সাহিত্য, ধর্ম দর্শন, বিজ্ঞান, যুক্তিনিষ্ঠা ভাবনা, ব্যক্তিস্বাতন্ত্র্যবাদী জীবন পদ্ধতি, প্রকৃতিবাদ ও মানবতাবাদী ভাবনার বিকাশ লক্ষ্য করা যায়। রামমোহন রায়ের ভাবনা ও কর্মে ইউরোপের নবজাগরণের প্রায় সকল বৈশিষ্ট্য লক্ষ করা যায়। ধর্মকে কেন্দ্র করেই আমাদের নবজাগরণের আন্দোলন প্রথম আত্মপ্রকাশ করেছিল। ধর্ম কেন্দ্রীক ভারতবর্ষে এটা স্বাভাবিক। কিন্তু ধর্মান্দলোনের মূল উদ্দেশ্য হল একটি সুস্থ জীবনাদর্শ প্রতিষ্ঠা, এই সত্য ভূলে ধর্মের বহিরঙ্গ আলোচনায় এবং বিভিন্ন ধর্মের তাত্ত্বিক বিচার বিশ্লেষণে মত্ত ছিল মধ্যযুগীয় ধর্ম বেত্ত্বাগণ। পুরোহিত তন্ত্রের প্রাধান্য ও তাদের বেদ ও শাস্ত্রের অপব্যাখ্যা, নানা আচার বিচার, কুসংস্কার জনগণের উপর চাপিয়ে দিয়ে অন্ধকারে নিমজ্জিত রাখা ছিল একমাত্র লক্ষ্য। ১৮২৮ সালে তিনি ব্রাহ্মসভা প্রতিষ্ঠা করেন, পরে তা ব্রাহ্মসমাজ নামে পরিচিত হয়। তিনি বিভিন্ন ধর্মগ্রন্থ অধ্যায়ণ করে উপলব্ধি করেন 'একেশ্বরবাদী' ধারণা। তিনি ইসলাম, খ্রীষ্টানধর্মের সঙ্গে বেদান্তের মিলন ঘটিয়েছেন। তিনি বহুধাবিভক্ত হিন্দুধর্মের সংস্কার করে বেদান্ত ধর্মকে জাতিয় ধর্ম হিসাবে প্রতিষ্ঠা করতে চেয়েছিলেন। তাঁর ধর্ম চিন্তার মূল কথা হলঃ এক ঈশ্বরের অস্তিত্বে বিশ্বাস, মানবপ্রীতি প্রকৃত আধ্যাত্মিকতার অঙ্গ, আত্মার সঙ্গে পরমাত্মার সম্পর্ক এবং অলৌকিক বা অতিপ্রাকৃত বিষসমূহের অসারতা এবং নিরাকার ঈশ্বরকে পৌত্তলিকতা ও অথহীন আচারে আবদ্ধ না করা।[১] তিনি তাঁর ব্রাহ্মসভাকে সকল ধর্মের মানুষের জন্য উন্মুক্ত করে দেন।

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In silico study reveals binding potential of rotenone at multiple sites of pulmonary surfactant proteins: A matter of concern

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ABSTRACT

Rotenone is a broad-spectrum pesticide employed in various agricultural practices all over the world. Human beings are exposed to this chemical through oral, nasal, and dermal routes. Inhalation of rotenone exposes biomolecular components of lungs to this chemical. Biophysical activity of lungs is precisely regulated by pulmonary surfactant to facilitate gaseous exchange. Surfactant proteins (SPs) are the fundamental components of pulmonary surfactant. SPs like SP-A and SP-D have antimicrobial activities providing a crucial first line of defense against infections in lungs whereas SP-B and SP-C are mainly involved in respiratory cycle and reduction of surface tension at air–water interface. In this study, molecular docking analysis using AutoDock Vina has been conducted to investigate binding potential of rotenone with the four SPs. Results indicate that, rotenone can bind with carbohydrate recognition domain (CRD) of SP-A, N-, and C- terminal peptide of SP-B, SP-C, and CRD of SP-D at multiples sites via several interaction mediators such as H bonds, C–H bonds, alkyl bonds, pi-pi stacked, Van der Waals interaction, and other. Such interactions of rotenone with SPs can disrupt biophysical and anti-microbial functions of SPs in lungs that may invite respiratory ailments and pathogenic infections.

1. Introduction

Pesticide pollution is a major global health concern. Indiscriminate application of pesticides has contaminated almost every component of the biosphere. Till date, numerous pesticides have been formulated. According to the target organism, pesticides are classified as herbicides, fungicides, insecticides, rodenticides, nematicides, and molluscicides. These chemicals target specific metabolic pathways in pests to control their population. However, they may interrupt various biomolecules in organisms other than pests to elicit toxic responses. Numerous studies have reported pesticide-induced oxidative stress, cytotoxicity, and organotoxicity on human and model organisms (Mandi et al., 2020; Khatun et al., 2018; Rajak et al., 2018; Sarkar et al., 2018; Nicolopoulou-Stamati et al., 2016; Podder and Roy, 2015; Rajak et al., 2015). Additionally, pesticide exposure can disrupt protein homeostasis and augment pathogenicity of infectious as well as fatal diseases (Rajak et al., 2021; Rajak and Roy, 2018).

Rotenone is a colorless, odorless and crystalline heteropentacyclic broad-spectrum insecticide derived from the roots and stems of *Lonchocarpus* and *Derris* species. It is lipophilic in nature and therefore can easily cross lipid bilayer of cells in several tissues. Rotenone is an established inhibitor of complex I of the mitochondrial electron

Abbreviations: ALA, Alanine; ARG, Arginine; ASN, Asparagine; ASP, Aspartic acid; CYS, Cysteine; GLN, Glutamine; GLU, Glutamic acid; GLY, Glycine; HIS, Histidine; ILE, Isoleucine; LEU, Leucine; LYS, Lysine; MET, Methionine; PHE, Phenylalanine; PRO, Proline; SER, Serine; THR, Threonine; TRP, Tryptophan; TYR, Tyrosine; VAL, Valine.

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3.2. Rotenone ~ SP-B interaction

Rotenone interacted with binding site 1 of N-terminal peptide of SP-B with affinity of −6.8 kcal/mol. ARG12 formed two conventional H-bonds of 2.099 Å and 2.208 Å length with rotenone. Other covalent interactions were also evident between rotenone and several amino acid residues.

Rotenone interacted with N-terminal peptide (binding site 2) of SP-B with affinity of −5.6 kcal/mol. Two H-bonds between ligand and ARG17 were noticed with bond length of 2.382 Å and 2.421 Å. ILE15 established Van der Waals interaction with the ligand. Further, Pi interactions were also recorded between rotenone and PHE1, LEU14, ILE18, and MET21 of SP-B.

Rotenone binds with C-terminal peptide of SP-B with various bonds and interactions. Amino acids such as MET3 and LEU4 formed H-bonds with rotenone. Bond lengths were measured as 2.567 Å for MET3 and 3.01 Å for LEU4. Pi interaction was established between ligand and ARG10 & LEU13 of SP-B. Affinity for C-terminal peptide of SP-B was recorded as −5.6 kcal/mol (Fig. 4).

3.3. Rotenone ~ SP-C interaction

Rotenone interacted with binding site 1 of SP-C with affinity of −5.8 kcal/mol. Three H-bonds were established between rotenone and ARG10 with bond length of 2.339 Å, 2.402 Å, and 2.434 Å. Alkyl and Pi-alkyl interactions were contributed by PRO9 and ARG12. Ligand established Van der Waals interaction and C–H bonds with SER1 and PRO3 respectively.

Interaction between binding site 2 of SP-C and rotenone was stabilized by conventional H-bond (bond length: 2.155 Å) shared by LYS23. Other interactions involved Pi interaction (ILE15, PRO19, VAL20, LEU22, LEU26) and Van der Waals interaction (PHE17). Affinity for binding site 3 was recorded as −5.5 kcal/mol.

Rotenone interacted with binding site 3 of SP-C using conventional H bond between ligand and ALA8 (bond length: 2.420 Å and 2.438 Å). C–H bond was shared between ligand and ALA7. Van der Waals interaction was stabilized by amino acid residues viz. PRO9, ARG10, and PRO16. ILE15 and PHE17 established other non-covalent interactions with the rotenone. Affinity for binding site 3 was recorded as −5.3 kcal/mol (Fig. 5).

3.4. Rotenone ~ SP-D interaction

Interaction between rotenone and binding site 1 (CRD) of SP-D was stabilized by three conventional H bonds shared by ASN288, ALA290, and ARG343. Other interactions included Van der Waals (GLU289, THR336, ARG349) and Pi interaction (GLU333, PHE335). Affinity was measured as −6.3 kcal/mol.

Rotenone can bind CRD (binding site 2) through conventional H bond (GLN258; bond length: 2.047 Å) and C–H bonds (SER294, SER298). Van der Waals interaction was stabilized between ligand and amino acids such as PHE254, MET295, THR296, TYR306, PRO307, THR305, and GLY309. Rotenone interacted with binding site 2 of SP-D with affinity of −6.3 kcal/mol.

Rotenone binds at neck region (binding site 3) of SP-D with two conversional H bonds shared between the ligand and amino acid ARG272 (bond length: 2.745 Å) and SER273 (bond length: 2.047 Å). Other interactions included Van der Waals (GLY241, GLU242, GLU354, PHE355) and Pi-interactions (GLU276, VAL240, LYS243, ALA275). Affinity for binding site 3 was recorded as −6.2 kcal/mol (Fig. 6).

Binding between rotenone and CRD domain (binding site 4) of SP-D was stabilized by one H-bond (ARG343), several Van der Waals interactions (GLU289, THR336, ARG349, GLU321, GLU329, ASN323, ASP325, ASN341), Pi-Pi interaction (PHE335) and other non-covalent interactions (GLU333, ALA-290). Affinity was measured as −6.0 kcal/mol.

Interaction of rotenone with CRD of SP-D at binding site 5 was mediated by two conventional H bonds. Amino acids ARG-272 and SER-273 participated in convensional H bond formation between SP-D and rotenone. GLY241, GLU242, and GLU354 were involved in Van der Waals interaction between protein and ligand. Binding of ligand was further stabilized by Pi-interactions stabilized by VAL240 and ALA275. Other non-covalent interactions were established by LYS243 and GLU276. Affinity for binding site 5 was recorded as −5.9 kcal/mol (Fig. 7). Table 1 represents hydrogen and hydrophobic interactions between SPs and ligand.

3.5. Affinity of rotenone and other pesticides for SPs

Molecular docking analyses have shown that rotenone has higher affinity for SPs compared to other pesticides (Table 2; Fig. 8). Rotenone showed 2–2.19 fold higher affinity than the dichlorvos, acephate, and ethion for SP-A. Affinity of rotenone for SP-B was 1.94–2.06 fold higher than the other three pesticides. Rotenone had 1.70, 1.81, and 1.87 fold greater affinity for SP-C when compared to dichlorvos, acephate, and ethion respectively. Rotenone showed higher affinity (1.70–1.96 fold) than dichlorvos, acephate, and ethion for SP-D.

4. Discussion

The present in silico study has revealed potential of rotenone to bind pulmonary surfactant proteins at multiple sites.

Rotenone was detected to interact with multiples sites of CRD of monomeric SP-A. Interactions were stabilized by conventional H bonds, C–H bonds, alkyl/pi-alkyl contacts and Van der Waals interaction between the ligand and the several amino acid residues of SP-A. CRD is critical to most SP-A mediated biophysical functions and is needed for maintenance of proper respiratory cycle. In addition, globular domain of CRD interacts with carbohydrate or other ligands of microbial pathogens in lungs and blocks further infection. For instance, CRD of SP-A binds with surface glycoprotein of *Pneumocystis carinii*, a common cause of life-threatening pneumonia and enhances adherence to alveolar macrophages (McCormack et al., 1997). It helps in neutralization, agglutination, and clearance of *Pneumocystis carinii*. SP-A acts as an important modulator of alveolar macrophage function that is required for enhanced capacity of phagocytosis of *Mycobacterium tuberculosis* (Gaynor et al, 1995). Respiratory syncytial virus (RSV) is the leading cause of bronchiolitis in developing world. Trimeric units of SP-A effectively neutralize RSV in human bronchial epithelial cells and reduce the level of infection (Watson et al., 2017). Moreover, SP-A via its Sialic acid residues functions as an opsonin in the phagocytosis of influenza A virus (H1N1 and H3N2) by alveolar macrophages (Benne et al., 1997; Benne et al., 1995). *Aspergillus fumigates* is an opportunistic fungal pathogen that causes allergic bronchopulmonary aspergillosis. Studies have clearly indicated that, SP-A interacts with the glycosylated antigens and allergens of *Aspergillus fumigates* and thereafter lowers risk of allergic reactions like high levels of IgG, IgE, blood eosinophilia, and extensive infiltration of lymphocytes (Madan et al., 2001). In another study, SP-A null mice was observed to be more susceptible to pulmonary fungal infection with *Histoplasma capsulatum* than age-matched wild-type control mice (McCormack et al., 2003). The increased susceptibility was associated with reduced number of $CD8^+$ cells in lungs of SP-A null mice. Carboxyl-terminal domain of SP-A containing C-type lectin CRD has antioxidant property. It directly protects surfactant phospholipids and macrophages from lipid peroxidation and oxidative cellular injury (Bridges et al., 2000). Thus, binding of rotenone to CRD at multiple sites can disrupt the interaction between SP-A and several microbial pathogens that can further result in exacerbated infection in alveoli

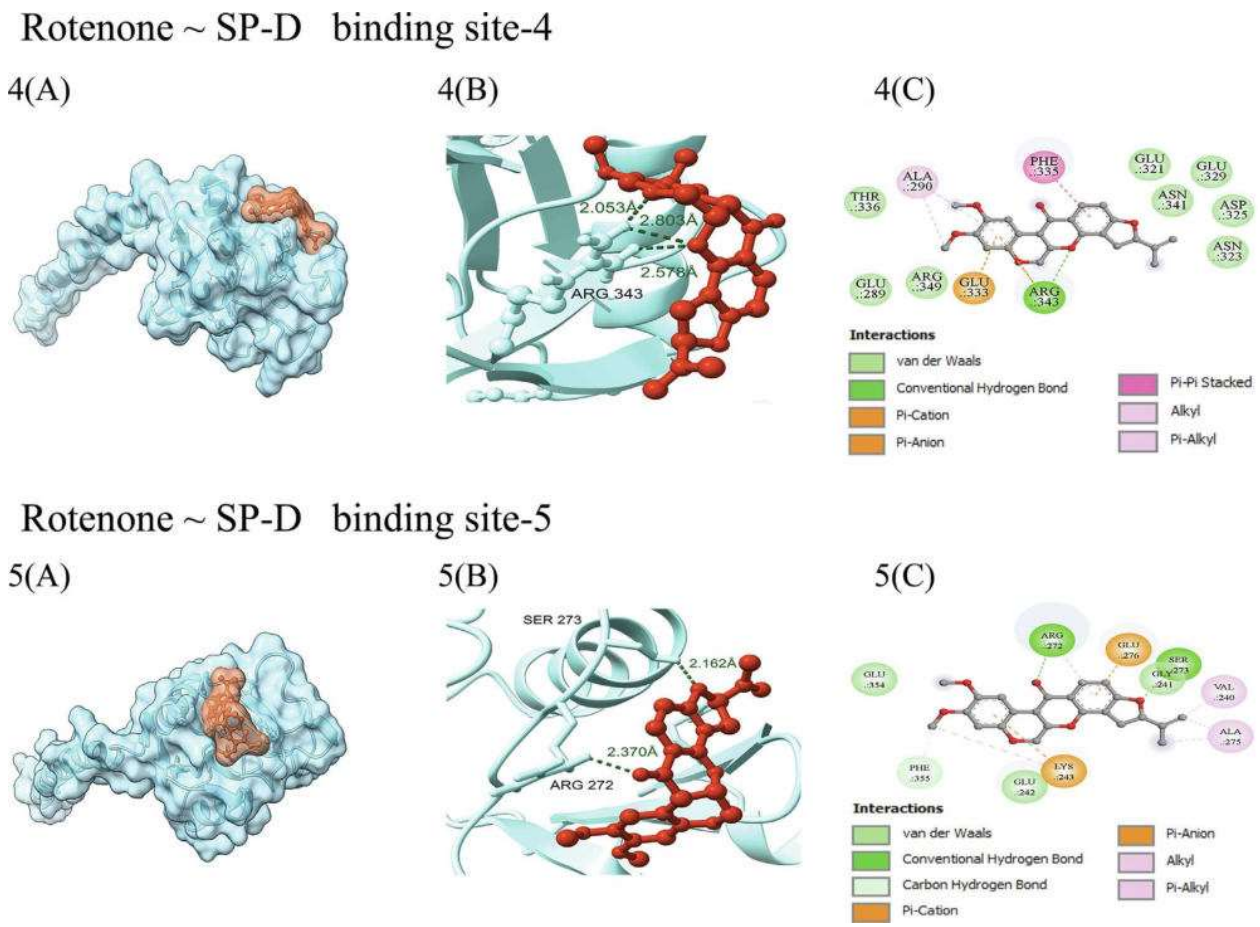

Fig. 7. The figure demonstrates binding of rotenone at binding site 4 and 5 of SP-D. Figure in first column (A) provides information regarding the binding of rotenone at a particular site of the protein. Column (B) represents H-bonds with bond length between the amino acid residues of protein and ligand. Column (C) represents all the polar and non-polar interactions between various amino acid residues of protein and ligand.

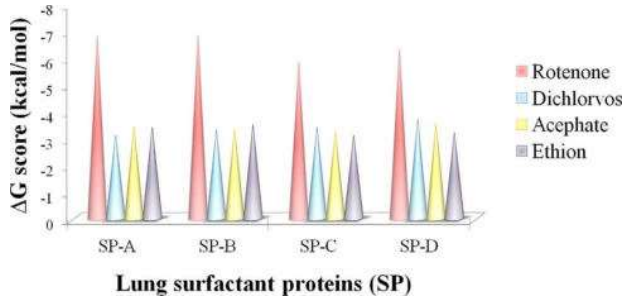

Fig. 8. Clustered cone diagram showing binding affinity of pesticides such as rotenone, dichlorvos, acephate, and ethion for surfactant proteins (SP-A, SP-B, SP-C, and SP-D). Cones indicate greater binding affinity (lower ΔG scores) of rotenone for SPs where as other pesticides show comparatively lower binding affinity (higher ΔG scores) for SPs.

cytokine release and subsequent lung tissue injury through different signaling pathways such as TLR4 (Arroyo and Kingma, 2021). SP-D inactivity in severe asthma is involved in disease persistence. SP-D enhances binding and internalization of allergen-containing sub-pollen particles with primary bronchial epithelial cells and facilitates their clearance (Schleh et al., 2010). Therefore, lack of functional SP-D may result in allergen-mediated breathing ailments. Importantly, phagocytosis and pulmonary clearance of RSV in airways are enhanced by SP-D as CRD recognizes RSV glycoproteins in a Calcium-dependent fashion (LeVine et al., 2004). Influenza virus is also targeted and opsonized by SP-D (White et al., 2008). Interestingly, recombinant fragment of human SP-D has been shown to interact with spike protein of SARS-CoV-2: the causative agent of ongoing pandemic disease coronavirus disease-19 (COVID-19) (Madan et al., 2021). In this study, recombinant fragment of human SP-D inhibited SARS-CoV-2 replication more efficiently than antiviral drug, Remdesivir. In another study, SP-D showed a dose-responsive binding to receptor binding domain and acted as entry inhibitor of SARS-CoV-2 pseudo-typed viral particles (Hsieh et al., 2021). These findings have suggested that, depletion in functional SP-D might result in increased susceptibility to COVID-19. SP-D also inhibits bacterial LPS-triggered inflammatory cell response (Atochina-Vasserman et al., 2010). Various ligands such as 1,3-β-D-glucan, 1,6-β-D-glucan, galactosaminogalactan galactomannan, glucuronoxylomannan, and mannoprotein 1 of pathogenic fungi are recognized by CRD that aids to fungicidal activity of SP-D (Madan and Kishore, 2020). It agglutinates *Aspergillus fumigatus conidia* and escalates uptake of opsonized conidia by alveolar macrophages and neutrophils (Madan et al., 1997). SP-D also binds with acapsular

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(ψ, ϕ)-Wardowski contraction pairs and some applications

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Abstract
In this paper, we propose the notion of (ψ, ϕ)-Wardowski contraction pairs and achieve a common fixed point theorem consistent with such kind of contractions in complete metric spaces. One of the main motivations of this article is to define a contractive condition which does not compel the mappings to be continuous at their common fixed points, an interesting question posed by Rhoades (Contemporary Math 72:233–245, 1988). Besides, we provide some applications of our obtained results in certain type of operator equations, fractional differential equation boundary value problems, functional equations arising in dynamic programmings, and a particular type of non-linear quadratic integral equations which are relevant to events arising in physics, economics, engineering, operations research, and many other relevant disciplines.

Keywords Common fixed points · (ψ, ϕ)-Wardowski contraction · Fractional differential equation · Dynamic programming · Quadratic integral equations

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which is impossible. This implies that

$$d(Tu, w) = 0 \Rightarrow Tu = w = Su,$$

and u is a coincidence point of S and T. Therefore, in all cases, u is a coincidence point of S and T.

To prove that u is the unique point of coincidence of S and T, let $v(\neq u)$ be another point of coincidence. Then, $Tu = Su$ and $Tv = Sv$. We have $d(u, v) = d(Tu, Tv) > 0$. Considering Definition 2.5, we have

$$\phi(d(Tu, Tv)) \leq \psi(\phi(M_{T,S}(u, v))), \tag{2.6}$$

where

$$\begin{aligned} M_{T,S}(u, v) &= \max\left\{d(Su, Sv), d(Su, Tu), d(Sv, Tv), \right. \\ &\quad \left. \frac{1}{2}\left[d(Su, Tv) + d(Tu, Sv)\right]\right\} \\ &= \max\{d(Su, Sv), 0, 0, \frac{1}{2}\left[d(Su, Sv) + d(Su, Sv)\right]\} \\ &= d(Su, Sv) \\ &= d(u, v). \end{aligned}$$

Now, from (2.6), we obtain

$$\begin{aligned} \phi(d(u, v)) &= \phi(d(Tu, Tv)) \\ &\leq \psi(\phi(d(u, v))) \\ &< \phi(d(u, v)), \end{aligned}$$

and we arrive at a contradiction. Hence, T and S have a coincidence point in $\mathcal{X}$. □

The subsequent example affirms our obtained result.

Example 2.7 Let $\mathcal{X} = \mathbb{R}$ be equipped with the metric $d(z, w) = |z - w|$. We define two mappings T and S by

$$Tz = \begin{cases} 0, & \text{when } z = 0; \\ z + 1, & \text{when } z \neq 0, \end{cases}$$

and

$$Sz = \begin{cases} 0, & \text{when } z = 0; \\ 3z + 1, & \text{when } z \neq 0. \end{cases}$$

Here, one can easily check that $T(\mathcal{X}) \subseteq S(\mathcal{X})$ and $S(\mathcal{X})$ is complete. Also, we take $\phi(t) = t$ and $\psi(t) = \alpha t$, where $\frac{1}{3} < \alpha < 1$. Now, we have two possible cases as follows:

Case-I: when $w = 0, z > 0$; then, $d(Tz, Tw) = d(Tz, T0) = d(z + 1, 0) = z + 1$, $\phi(z + 1) = z + 1$.

We have

$$\begin{aligned} M_{T,S}(z, 0) &= \max\left\{d(Sz, S0), d(Sz, Tz), d(S0, T0), \frac{1}{2}\left[d(Sz, T0) + d(Tz, S0)\right]\right\} \\ &= \max\left\{d(3z + 1, 0), d(3z + 1, z + 1), d(0, 0), \frac{1}{2}\big[d(3z + 1, 0) \right. \\ &\quad \left. + d(z + 1, 0)\big]\right\} \end{aligned}$$

Now, we deliver the ensuing result concerning the existence and uniqueness of solution to the boundary value problem.

Theorem 4.3 *Let us consider the boundary value problem (4.1), (4.2) and assume that any one of the following conditions hold:*

$(F1)$ *there exists a real number* β *with* $0 \leq \beta < 1$, *such that*

$$|f(\zeta, u(\zeta)) - f(\zeta, v(\zeta))| \leq \beta |f(\zeta, u(\zeta))| - \beta \sup_{0 \leq \tau \leq 1} |u(\tau)|$$

for all real-valued continuous functions $u(\zeta), v(\zeta)$ *defined on* $[0, 1]$, *and* $\lambda K_1 \geq 1$;

$(F2)$ *there exists a real number* β *with* $0 \leq \beta < 1$, *such that*

$$|f(\zeta, u(\zeta)) - f(\zeta, v(\zeta))| \leq \beta |u(\zeta) - v(\zeta)|$$

for all real-valued continuous functions $u(\zeta), v(\zeta)$ *defined on* $[0, 1]$, *and* $\lambda K_0 \leq 1$.

Then, the problem has a unique solution in $C[0, 1]$.

Proof Let us consider the complete metric space $(C[0, 1], d)$, where d is the sup metric. We define a self-map T on $C[0, 1]$ by

$$(Tu)(\tau) = \lambda \int_0^1 G(\tau, \zeta) f(\zeta, u(\zeta)) \mathrm{d}\zeta$$

for all $u \in C[0, 1]$ and $\tau \in [0, 1]$. Then, the fixed point(s) of T is the solution(s) of the boundary value problem (4.1), (4.2). First, we assume that condition $(F1)$ holds. Then, we have

$$\lambda G(\tau, \zeta) |f(\zeta, u(\zeta)) - f(\zeta, v(\zeta))| \leq \beta \lambda G(\tau, \zeta) |f(\zeta, u(\zeta))| - \beta \lambda G(\tau, \zeta) \sup_{0 \leq \tau \leq 1} |u(\tau)|.$$

Hence

$$\int_0^1 \lambda G(\tau, \zeta) |f(\zeta, u(\zeta)) - f(\zeta, v(\zeta))| \mathrm{d}\zeta \leq \int_0^1 \beta \lambda G(\tau, \zeta) |f(\zeta, u(\zeta))| \mathrm{d}\zeta - \int_0^1 \beta \lambda G(\tau, \zeta) \sup_{0 \leq \tau \leq 1} |u(\tau)| \mathrm{d}\zeta$$

and

$$\begin{aligned}
&\int_0^1 |\lambda G(\tau, \zeta) f(\zeta, u(\zeta)) - \lambda G(\tau, \zeta) f(\zeta, v(\zeta))| \mathrm{d}\zeta \\
&\leq \int_0^1 \beta \lambda G(\tau, \zeta) |f(\zeta, u(\zeta))| \mathrm{d}\zeta \\
&- \int_0^1 \beta \lambda K_1 \sup_{0 \leq \tau \leq 1} |u(\tau)| \mathrm{d}\zeta \\
&\leq \int_0^1 \beta \lambda G(\tau, \zeta) |f(\zeta, u(\zeta))| \mathrm{d}\zeta - \beta \lambda K_1 |u(\tau)| \\
&\leq \int_0^1 \beta \lambda G(\tau, \zeta) |f(\zeta, u(\zeta))| \mathrm{d}\zeta - \beta |u(\tau)| \\
&\leq \beta \left| \int_0^1 \lambda G(\tau, \zeta) f(\zeta, u(\zeta)) d\zeta - u(\tau) \right|. \qquad (4.3)
\end{aligned}$$

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पूर्वबर्धमानः, पश्चिमबङ्गः, भारत

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मधुसूदनसरस्वतीप्रणीते कृष्णकुतूहलनाटके श्रीकृष्णः

समीरणः रायः

शोधसारः
गौडीयवैष्णवसाहित्ये मधुमूदनमरस्वत्या एकं विशिष्टमवदानं वर्तते। प्रख्यातपण्डितो दार्शनिकः परमभक्तः सन्न्यासी श्रीमधुसूदनसरस्वती बांलादेशे फरिदपुरजिलान्तर्गते कोटालिपाडापररगणास्थिते ऊनशिया इति ग्रामे अजायत। ईशवीयः षोडश-सप्तदशशतकः तस्य समयकालः। सर्वतन्त्रपारङ्गमस्य तस्य मातुर्नाम अरुन्धतीदेवी पिता च प्रमोदन-पुरन्दराचार्य-नारायणः। सन्न्यासग्रहणात्पूर्वं तस्य नाम आसीत् कमलनयनः। अद्वैतवेदान्ती मधुसूदनसरस्वती अद्वैतसिद्धिः, अद्वैतरत्नरक्षणम्, भक्तिरसायनम् इत्यादीनि ग्रन्थानि रचयित्वा वैष्णवसाहित्यं तथा संस्कृतसाहित्यं समृद्धमकरोत्। परं कृष्णकुतूहलमिति नाटकं तस्य कीर्तिकेतुं वहति। नाटकस्यास्य राधाकृष्णयोरपार्थिवलीलास्वादनेन आह्लादिता भवन्ति सहृदयाः।
कृष्णकुतुहलं सप्ताङ्कविशिष्टमेकं नाटकम्। राधाकृष्णयोः चन्द्रावली-कृष्णयोर्गोपिकासु च कृष्णस्य लीलावर्णनेन भक्तिरसस्य प्रतिपादनमेव नाट्यकारस्य मुख्याशयः। नाटकेऽस्मिन् नायकः श्रीकृष्णः, नायिका श्रीराधाः प्रतिनायिका च श्रीचन्द्रावली। श्रीमद्भागवत्-पद्मपुराणात्मके अस्मिन्नाटके न केवलं कृष्णस्य कैशोर-यौवनविषयकस्य वर्तमानचरितस्य, अपि तु कंसवधरूपस्य भाविचरितस्य वर्णनमस्ति। एवंविधस्य कृष्णकुतूहलनाटकस्य मधुसूदनसरस्वतीचित्रितस्य श्रीकृष्णचरित्रस्य समीक्षात्मकमध्ययनं शोधप्रबन्धेऽस्मिन् विधीयते।

कूटशब्दाः – कृष्णकुतूहलम्, श्रीकृष्णः, मधुसूदनसरस्वती।

प्रस्तावना

गौडीयवैष्णवसाहित्ये मधुसूदनसरस्वत्या एकं विशिष्टमवदानं वर्तते। प्रख्यातपण्डितो दार्शनिकः परमभक्तः सन्न्यासी श्रीमधुसूदनसरस्वती बांलादेशे फरिदपुरजिलान्तर्गते कोटालिपाडापररगणास्थिते ऊनशिया इति ग्रामे अजायत। परन्तु तस्य कर्मभूमिरासीत् मुक्तिनगरी वाराणसी। ईशवीयः षोडश-सप्तदशशतकः तस्य समयकालः। सर्वतन्त्रपारङ्गमस्य तस्य मातुर्नाम अरुन्धतीदेवी पिता च प्रमोदन-पुरन्दराचार्य-नारायणः। सन्न्यासग्रहणात्पूर्वं तस्य नाम आसीत् कमलनयनः। अद्वैतवेदान्ती मधुसूदनसरस्वती अद्वैतसिद्धिः, परमहंसप्रियाख्यागीताव्याख्या, सिद्धान्तबिन्दुः, वेदान्तकल्पलतिका,

नारदप्रणीतं गर्भनाटकं दृष्ट्वा प्रीत्वा च नाटकस्य कुशीलवानां नाट्यकारनारदस्य च अभीष्टं प्रदत्तवान्। श्रीकृष्णानुग्रहे एव गन्धर्वसुदर्शनः शापात् मुक्तिं लब्धवान्। श्रीकृष्णः सुदक्षः मल्लयोद्धापि, मल्लयुद्धेनैव चाणूरं हन्ति। सुमधुरसुरसृष्टौ तस्य दक्षता प्रश्नातीता। तस्य मुरलाध्वनेः माहात्म्यं वर्णयन्ति राधासख्यः –

पीयूषं विषयन् विषं च सुधयन् निर्जीवितं जीवयन्
सञ्जातः कुलजायशोद्रिकुलिशः कोऽप्येष वंशीस्वनः॥"[9]

एषा वंशीध्वनिः कर्णपथमाध्यमेन हृदयं प्रविष्ट्वा गोपरमणीः आकुलीकरोति, तेऽपि कुलं, मानं, यशं, पतिप्रेमानं सर्वं तुच्छं कृत्वा उपस्थिताः जाताः कृष्णसम्मुखे। एतानि सर्वाणि चारित्रिकवैशिष्ट्यानि अतिक्रमं करोति कृष्णस्य प्रेमिकस्वरूपः। द्वितीयाङ्के वृन्दावनशोभादर्शनावसरे अनङ्गसेना-कमलमाला-चम्पककलिका-कामाङ्कुराप्रमुखाः गोपवालाः प्रति आसक्तः सस्पृहः कृष्णः तेषां नामानाम् अन्वयार्थौ विचारपूर्वकं वर्णयति –

"यत्पत्युपचितलक्ष्मीरथगजलीलातुरङ्गसम्पत्तिः।

तथा च कमलमालायाः अपि वर्णनं कृतं तेन –

"चरणौ कमले कमले च करौ युगलं कुचयोरपि तन्मुकुले।
वदनं कमलं नयने कमले सुतनोः कमलान्यखिलैव तनुः॥"
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गोपीगणापि कृष्णप्रेमनि उन्मत्ताः। श्रीकृष्णं पतित्वेन प्राप्तुं ते कात्यायणीपूजां कुर्वन्ति। कृष्णदर्शनमपि येषां समीपे परमसौभाग्यं ताः गोपवनिताः कृष्णकृपालाभे न वञ्चिताः। मुरलीध्वन्या आह्वानं कृत्वा रासलीलायां ताः परमानन्दं ददाति, कालेऽस्मिन् वाधास्वरूपं भद्रमुखं गृहे प्रेरणेऽपि श्रीकृष्णः अकुण्ठितः। चन्द्रं तिरस्कर्तुं समर्था यस्याः वदनचन्द्रिका तां चन्द्रावलीं दृष्टा श्रीकृष्णः तां प्रति आकृष्टं भवति अपि च एतावत् पर्यन्तं तस्याः अदर्शनाय आक्षेपयति –

"व्यामोहयति भुजङ्गानङ्गीकुरुते महत्तमं ज्योतिः।
अतनुविषज्वरहरणी रमणी किमियं महामणिश्रेणी॥"[11]

श्रीकृष्णदर्शनमात्रे चन्द्रावली अपि मोहिता जाता। अनङ्गसेनादीनां गोपीनामपेक्षया चन्द्रावलीं प्रति श्रीकृष्णस्य प्रेमासीत् समधिकमेव। सः चन्द्रावलीकुञ्जे चन्द्रावल्या सह सहास्यपरिहासं वर्षासुषमां पश्यति। चन्द्रावल्याः कोपप्रशमनाय स्वं दासरूपेण उल्लिखितम्, तस्याः पदाघातं प्रार्थितं तथा निःसङ्कोचेन चन्द्रावलीचरणतले पतितम्। अपि च कन्दर्पहर्षस्वरूपां श्रीराधां दृष्ट्वा तामपि वर्णितं तेन श्रीकृष्णेन –

"कराङ्घ्रिमुखलोचनं नयनरञ्जनं नीरजैर्वपुः प्रकृतिसुन्दरं
कनकचम्पकैः कल्पितम्।
स्तनद्वयमनुत्तमं स्तवकसम्पदा स्वस्तरोर्धनं
कुसुमधन्वनस्तादिह राधिकैवाधिकम्॥"[12]

कृष्णहृदयः व्याकुलं भवति राधाहृदयसंवादनिमित्ताय। हृदयाद् आरभ्य अपरहृदये यद् समाप्तं भवति तदेव प्रेम। हृदयानन्दप्रदायिन्याः राधिकायाः विरहवशात् श्रीकृष्णः प्राणधारणे अक्षमः। प्रियतमायाः मनोभावं ज्ञात्वा आश्वस्तः जातः सः। क्षणमात्रविरहोऽपि परस्परयोः समीपे असहनीया प्रतिभाता। रासलीलायां श्रीकृष्णः प्राणधिकप्रियां ददाति सर्वाधिकसौभाग्यम्। अतः एकाधिके प्रियायां आसक्तः सन् अपि माधवः एकान्ततः राधायाः, श्रीराधिकायां निवेदितः। राधाकृष्णयोर्मधुरलीला यद्यपि संस्कृतसाहित्ये तथा भारतीयजनमानसे सुप्रसिद्धा तथापि नाट्यकारः मधुसूदनसरस्वती तस्य अपूर्ववस्तुनिर्माणक्षमाप्रतिभया तामभिनवरूपेणैव उपस्थापितवान्, यः न्यूनमाकर्षयति सहृदयचित्तम्। सन्न्यासी परमहंसपरिव्राजकाचार्यः परमभक्तः सन् अपि स्वनाटके अपार्थिवां कृष्णलीलां ग्रथयित्वा सहृदयहृदये स्फुटयति कृष्णप्रेम। अतः कृष्णकुतूहलनाटके श्रीकृष्णः मूलतः नाट्यकारस्य स्वस्य कवित्वशक्तिना निर्मितः।

ग्रन्थपञ्जी

1. कृष्णकुतूहलम् – लेखकः मधुसूदनसरस्वती, सम्पादकः हरिशङ्करओझा, सम्पूर्णानन्दसंस्कृतविश्वविद्यालयः, वाराणसी, प्रथमसंस्करणम्, १९९०।

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Understanding the cross-talk between mediators of infertility and COVID-19

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ABSTRACT

COVID-19 is the ongoing health emergency affecting individuals of all ages around the globe. Initially, the infection was reported to affect pulmonary structures. However, recent studies have delineated the impacts of COVID-19 on the reproductive system of both men and women. Hence, the present review aims to shed light on the distribution of SARS-CoV-2 entry factors in various reproductive organs. In addition, impacts of COVID-19 mediators like disrupted renin angiotensin system, oxidative stress, cytokine storm, fever, and the mental stress on reproductive physiology have also been discussed. For the present study, various keywords were used to search literature on PubMed, ScienceDirect, and Google Scholar databases. Articles were screened for relevancy and were studied in detail for qualitative synthesis of the review. Through our literature review, we found a multitude of effects of COVID-19 mediators on reproductive systems. Studies reported expression of receptors like ACE-2, TMPRSS2, and CD147 in the testes, epididymis, prostrate, seminal vesicles, and ovarian follicles. These proteins are known to serve as major SARS-CoV-2 entry factors. The expression of lysosomal cathepsins (CTSB/CTSL) and/ neuropilin-1 (NRP-1) are also evident in the testes, epididymis, seminal vesicles, fallopian tube, cervix, and endometrium. The binding of viral spike protein with ACE-2 was found to alter the renin-angiotensin cascade, which could invite additional infertility problems. Furthermore, COVID-19 mediated cytokine storm, oxidative stress, and elevated body temperature could be detrimental to gametogenesis, steroidogenesis, and reproductive cycles in patients. Finally, social isolation, confinement, and job insecurities have fueled mental stress and frustration that might promote glucocorticoid-mediated subnormal sperm quality in men and higher risk of miscarriage in women. Hence, the influence of COVID-19 on the alteration of reproductive health and fertility is quite apparent.

Contents

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Box 2. SARS-CoV-2 mediated Cytokine storm.

Infection with SARS-CoV-2 causes a cytokine storm that can lead to organ damage. The S1 subunit of the viral spike protein interacts with TLR7/8 to recruit downstream adaptors (MyD88, IRAK 4/1, and TRAF6). TRAF6 with dimeric ubiquitin conjugating enzyme complex (Ubc13-Uev1A) activates TAK1/TAB1/2 and IKKα/IKKβ. IKKα/IKKβ phosphorylates Ikβ to promote the nuclear translocation of NF-kβ involved in the transcription of various proinflammatory cytokines responsible for the cytokine storm. Endosomal dsRNAs through TLR3/4 are also implicated in the direct activation of NF-kβ through the recruitment of adaptor proteins namely TRIF, TRAF6, and RIP1. PAMPs and damage associated molecular patterns (DAMPs) also interact with NLRP3 to assemble procaspases-1 and ASC (apoptosis-associated speck-like protein containing CARD) into a multimeric component i.e. inflammasome. Activated caspase-1 cleaves proIL1β and proIL18 to generate the active version of proinflammatory cytokines. In addition, caspase-1 cleaves Gasdermin-D at Asp276 to separate N- and C-terminus domains. Active N-termini create pores in lipid bilayer to elicit pyroptosis and subsequent organ damage. Intense inflammation invites epididymal and testicular immunopathologies in men whereas impairs ovulation and endometrial receptivity in females.

Aberrant expression of IL10 in decidual T-lymphocytes is evident in women with recurrent miscarriage [71]. Dysregulation of inflammatory mediators are known to promote endometriosis-associated reproductive failure [72]. Cyclooxygenase 2 (COX2) production is enhanced by cytokines, and inhibitors of COX2 are implicated in treatment of dysmenorrhoea and heavy menstrual blood loss [73]. This indicates the possible contribution of COX2 to female infertility. Moreover, COX2 has links with endometrial carcinomas [74]. Finally, synthesis of Prostaglandin E2 (PGE2) is triggered by proinflammatory cytokines [75]. Dysregulated PGE2 is responsible for menorrhagic endometrium and excessive menstrual bleeding in women [76,77].

Therefore, the above suggested that cytokine storms caused by COVID-19 could be detrimental to the reproductive organs and reproductive physiology of both men and women.

4.3. Oxidative stress and disturbed reproductive health

Oxidative stress (OS) is a physiological condition in which the redox equilibrium is disrupted as a result of excessive reactive oxygen species (ROS) production at the subcellular level. SARS-CoV-2 mediated disruption of the RAS can lead to accumulation of ANG-II in blood plasma, and then promote ROS production via the NADPH oxidase (NOX)-protein kinase C (PKC) dependent pathway (Box 3) [78]. Hypoxia is a common symptom of COVID-19 and it acts as a stimulant for ROS generation [79]. Meta-analysis of 1210 COVID-19 cases has revealed reduced hemoglobin levels (5.9 g/L-7.1 g/L) [80] which might be related to anemic hypoxia and cellular ROS production in patients.

The nuclear factor erythroid 2–related factor 2 (Nrf2) is a transcription factor that maintains redox balance in a living system. Respiratory viruses can abrogate the Nrf pathway to impose OS [81]. Moreover, proinflammatory cytokines can increase ROS production [82], putting redox-equilibrium in jeopardy. Excessive production of ROS and disturbed antioxidant defense machinery have been found to be evident during coronavirus infection [83]. Some researchers have argued that coronavirus induced lung injury is triggered by OS and NF-kB signaling in patients [84].

Excessive ROS and subsequent OS in male gonads can impair genesis, motility, and fertilization capacity of mature sperms. Surprisingly, a Canadian research group has discovered substantial ROS generation in 40 % of the semen collected from infertile men [85]. Related to this, the cell membranes of spermatozoa are rich in polyunsaturated fatty acids (PUFAs) that are extremely vulnerable to ROS-induced lipid peroxidation (LPO). LPO promotes the disruption of membrane fluidity and the rapid loss of ATP from spermatozoa, leading to axonal damage, midpiece defects, and reduced sperm motility and viability [86]. Excessive ROS is also positively correlated with varicocele in men [87], which is a leading cause of male infertility.

Other effects of ROS and OS on male gonads have also been observed. For example genetic materials of spermatozoa are highly vulnerable to ROS-induced base modification and degradation [88]. Single or double stranded DNA breaks in gametes can lower the reproductive potential of fertile men. Moreover, infertile men with greater ROS levels tend to have more apoptotic spermatozoa than control individuals [89]. Massive ROS also impairs sperm motility, morphology, and ability to penetrate oocytes [90], and Sertoli cells injured by ROS lead to decreased sperm count and motility [91]. Additionally, Steroidogenesis is sensitive to redox dyshomeostasis and increases in the activities of COX2 and MAPK [92], and chemicals inducing ROS production impede testosterone synthesis in Leydig cells [93,94]. Finally, OS promotes long-term changes in epididymis and maturing spermatozoa resulting in declined sperm quality [95].

Optimum levels of ROS are implicated in the proper maintenance of female reproductive health. However, recent studies have

Box 3. NOX and Nrf cascades linked to Oxidative Stress.

The interaction between ANG-II and AT_1R triggers PKC and Src kinase mediated signaling pathways. PKC activates NOX, which is involved in ROS production. NOX is a multimeric protein composed of two membrane subunits (gp91-*phox,* p22-*phox*), three cytosolic subunits (p47-*phox*, p67-*phox*, p40-*phox*), and one G-protein *Rac*. Glycoprotein (gp)91-*phox* is NOX-2 specific and its homologs (DUOX1 and DUOX2) are detected in NOX-1, 3, 4, and 5. PKC phosphorylates p47-*phox* to facilitate its binding with the p67-*phox*/p40-*phox* complex. A trimeric complex is thus formed that translocates to the cell membrane and interacts with p22-*phox*. Src kinase activates *Rac* which independently move to the membrane and forms the active NOX complex. NOX then oxidizes molecular Oxygen into ROS. Nrf2 is a transcription factor, playing crucial role in redox-homeostasis. The activity of Nrf2 is regulated by Keap1 (Kelch-like ECH-associated protein-1) via cullin-3 dependent proteosomal degradation. Several kinases (PKC, PI3K/Akt, GSK-3β, JNK) phosphorylate Nrf2 and block its degradation. Phosphorylated Nrf2 then translocates into the nucleus and forms a heterodimer with Maf (masculoaponeurotic-fibrosarcoma) to bind antioxidant response elements (AREs) on nuclear DNA. AREs are implicated in the synthesis of endogenous antioxidants that alleviate OS. Respiratory viral infections can inhibit Nrf2 signaling and therefore promote ROS production and subsequent OS in host.

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Ecosystem modelling to understand the trophic dynamics and ecosystem health of a small tropical Indian estuary

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ABSTRACT

Estuaries provide enumerable ecosystem services to mankind in terms of provisional, regulating, supporting, recreational and information services. However, the persistent human-environment interactions for these services altered the ecological integrity of estuaries. Although the small estuaries receive little attraction in scientific studies due to their low surface area and regional importance, these ecosystems are more vulnerable to anthropogenic pressures and require urgent attention from the scientific fraternity. The Terekhol Estuary (TRE) is a small tropical estuary situated along Goa, west coast of India, gaining recognition in recent years due to the pollution risk from tourism activities. Moreover, the estuary also behaves as an extension of the marine realm during the dry season. The food web structure and network flow indices of the TRE was assessed to reveal its present ecological status. The Ecopath modelling approach was employed to delineate the ecosystem structure and trophic functioning of the estuary distributed in 22 ecological compartments from 2018 to 2019. The trophic level of the food web ranged from detritus (TL-1) to sharks (TL- 4.53). The ecosystem structure demonstrated a grazing chain (herbivory) based organization over the detritus-based pathway. The proportion of exports to the total flows was 35% for the TRE. The model has a high total system throughput (12,043.6 t km^{-2} $year^{-1}$), low system omnivory index (0.17) and connectance index (0.21), and a moderate relative ascendency (45.1%). Finn's cycling index (2.17%) indicated very low recycling in the system. All these indicators along with the eco-exergy index (8567.22 g detritus equivalent m^{-2}), specific eco-exergy (38.25) and robustness index (0.11) classified the estuary as be immature, less stable and less organized and is in the initial stages of its development. The ecological indicators analyzed here point towards a medium to a high level of impact in the TRE due to anthropogenic activities. We also highlight the management measures to be implemented in order to restore the ecological quality of the TRE.

1. Introduction

Estuaries are transitional systems that provide ecosystem services in the form of material resources (fish, sand, silt, etc.), tourism, navigation routes, recreation and culture, water quality regulation, and carbon sequestration (Beck et al., 2001). Estuaries function as nursery habitats, migration channels, and reproduction sites for fish and other aquatic organisms (Elliott et al., 2007; Nicolas et al., 2010). They also provide foraging habitats for aquatic species at all levels of the trophic hierarchy and offer fisheries resources to traditional fisherfolk living on the banks of these ecosystems (Beck et al., 2001; Cabral et al., 2007; Sreekanth et al., 2020a). However, these ecosystems are under stress all over the world because of various anthropogenic pressures such as overfishing, pollution, and habitat destruction (Coates et al., 2007; Diaz and Rosenberg, 2008; Elliott et al., 2007; Lal et al., 2021). The ecological functioning of an estuary is supported by diverse functional groups and their complex trophic interactions with each other, which ultimately reflects the ecosystem integrity (Lal et al., 2021; Lobry et al., 2008;

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Table 2 (*continued*)

Group name	Value	Reference
P/B	1.4 year^{-1}	Estimation from empirical formula, data from current study
Q/B	7.1 year^{-1}	Estimation from empirical formula, data from current study
EE	0.71	Estimation from Ecopath
Diet composition	79 samples	Current study and field sampling
17 Large pelagics		
B	0.03 t km^{-2}	Estimation from empirical formula, data from current study
P/B	2.1 year^{-1}	Estimation from empirical formula, data from current study
Q/B	6.9 year^{-1}	Estimation from empirical formula, data from current study
EE	0.53	Estimation from Ecopath
Diet	96 samples	Current study and field sampling
18 Small benthic carnivores		
B	0.55 t km^{-2}	Estimation from empirical formula, data from current study
P/B	3.1 year^{-1}	Estimation from empirical formula, data from current study
Q/B	16.73 year^{-1}	Estimation from empirical formula, data from current study
EE	0.91	Estimation from Ecopath
Diet	386 samples	Current study and field sampling
19 Jellyfish		
B	1.13 t km^{-2}	Duan et al. (2009); Sreekanth et al. (2020a)
P/B	2.70 year^{-1}	Duan et al. (2009); Sreekanth et al. (2020a)
Q/B	21.4 year^{-1}	Duan et al. (2009); Sreekanth et al. (2020a)
EE	0.49	Duan et al. (2009); Sreekanth et al. (2020a)
Diet	76 samples	Current study and field sampling
20 Sharks		
B	0.04 t km^{-2}	Estimation from empirical formula, data from current study
P/B	0.03 year^{-1}	Estimation from empirical formula, data from current study
Q/B	14.22 year^{-1}	Estimation from empirical formula, data from current study
EE	0.33	Estimation from Ecopath
Diet	75	Current study and field sampling
21 Birds		
B	0.001 t km^{-2}	Mohamed et al. (2008); Sreekanth et al. (2020a)
P/B	0.04 year^{-1}	Mohamed et al. (2008); Sreekanth et al. (2020a)
Q/B	19.51 year^{-1}	Mohamed et al. (2008); Sreekanth et al. (2020a)
EE	0.00	Estimation from Ecopath
Diet		Etezadifar and Barati (2011); Sivaperuman and Javson (2011)
22 Detritus		
B	200 t km^{-2}	Estimation from empirical formula, data from current study
EE	0.07	Estimation from Ecopath

B: biomass, P/B: production/biomass, Q/B: consumption/biomass, and EE: ecotrophic efficiency.

were averaged over the sampling sites and over the 2 years (2018 and 2019), and biomass was expressed in tonnes per square kilometre.

2.5. Birds

The major species of aquatic birds identified from the estuary were Great Egret (*C. albus*), Western Reef Egret (*E. gularis*), and Little Cormorant (*Phalacrocorax niger*). For birds, B, P/B and Q/B values were collected and modified from those for similar ecosystems (Duan et al., 2009; Mohamed et al., 2008; Pitcher et al., 2002; Rybarczyk and Elkaïm, 2003; Sreekanth et al., 2020a). The diet composition for these species was collected from secondary sources. The diet and feeding habit data for Great Egret, Little Cormorant, and Western Reef Egret were collected from published literature from the estuarine wetlands of Kerala, India (Sivaperuman and Javson, 2011) and Hara Biosphere Reserve, Persian Gulf (Etezadifar and Barati, 2011). Expert ecological knowledge of ornithologists and enthusiasts was also used in determining the diet composition of birds.

2.6. Zooplankton

Zooplankton density was recorded as the number of individuals per cubic metre of water and was used for arriving at the biomass values based on the average weight of individuals calculated using image analysis (Alcaraz et al., 2003); P/B values were calculated from the empirical formula used by Selleslagh et al. (2012) using the weighted average individual body weight (W) of the subgroups:

$$\frac{P}{B} = 0.6457 \times W^{-0.37} \quad (5)$$

Values of Q/B for zooplankton were collected from published sources (Mohamed et al., 2008; Sreekanth et al., 2020a, 2020b) and modified as required.

2.7. Phytoplankton and benthic producers

The sampling sites for phytoplankton were marked in the estuary map, and we collected the samples during the dry saline phase in 2018 (December and March) and 2019 (December and March). The phytoplankton was sampled from surface waters of the estuary at high tide ±2 h and the samples were fixed using 1% Lugol's iodine solution. The density was used for calculating the biomass after obtaining the weighted average individual body weight for each subgroup (diatoms, dinoflagellates, and blue-green algae) (Mahlmann et al., 2008; Wang and Seibert, 2017; Wasmund et al., 2017). The biomass of benthic producers and P/B values for phytoplankton and benthic producers were collected from published sources (Mohamed et al., 2008; Sreekanth et al., 2020a) and modified as required.

2.8. Jellyfish

The values of biomass, P/B, and Q/B for jellyfish were collected from secondary sources (Duan et al., 2009; Sreekanth et al., 2020a).

2.9. Heterotrophic and sessile benthos

Heterotrophic and sessile benthos were sampled at high tide ±2 h using a Van Veen grab (sampling an area of about 250 cm^2 to a sediment depth of about 10 cm), preserved in polythene bags, transported to the laboratory, and washed and gently sieved over a 1 mm mesh. All organisms were stained with Rose Bengal and preserved in 5% formaldehyde buffer for subsequent identification and their biomass was recorded. For benthic groups, the P/B values were calculated using the formula P/B = 0.6547 W$^{-0.37}$, where W is the weighted average individual body weight of the benthos components; Q/B values for the benthos component were collected from other similar Ecopath models (Mohamed et al., 2008; Selleslagh et al., 2012; Sreekanth et al., 2020a) and modified as required.

2.10. Detritus

The biomass of detritus was calculated using the empirical equation from the primary production (PPR) data collected from the chlorophyll-*a* method (APHA, 2005) from the sampling sites mentioned in the study area and euphotic depth suggested by Christensen and Pauly (1993):

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GENERALIZED QUASI-CONTRACTIONS ON WEAK ORTHOGONAL METRIC SPACES

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Abstract. In this sequel, we introduce and study the concept of the weak orthogonal metric spaces as a generalization of the orthogonal metric spaces. Besides, we define and study the generalized quasi-contractions on such spaces and illustrate several non-trivial examples to endorse our obtained results. Among other things, as corollaries we obtain the main results of some of the pioneering articles existing in the literature. Finally, we answer the open question posed by Gordji et al. [On orthogonal sets and Banach fixed point theorem, Fixed Point Theory, 18(2):569-578, 2017].
Key Words and Phrases: Weak orthogonal relation, orthogonal metric space, orbital O_w-continuity, Banach $\perp$-contraction, fixed point.
2020 Mathematics Subject Classification: 47H10, 54H25.

1. Introduction and preliminaries

Let (X, d) be any metric space and let T be a self-mapping on X. Then the set $Fix(T) = \{x \in X : Tx = x\}$ is the fixed point set of T. An operator T is said to be a contraction on X if

$$d(Tx, Ty) \leq rd(x, y)$$

holds for all $x, y \in X$ and for some $r \in [0, 1)$. The well-known Banach contraction principle [3] states that if T is a contraction on a complete metric space X, then T has only one fixed point.

Over the years, the metric fixed point theory has enthralled many a number of mathematicians in finding new theories, solving many real-life phenomena and therefore, a considerable number of research articles were put in print where the generalized versions of the metric notion are investigated by making alterations to the basic metric axioms. Eventually, there are a handful of metric structures which have come into

Proof. **(A)** We consider a sequence (x_n) in X such that $x_n = 1 - \frac{1}{n+1}$ for all $n \in \mathbb{N}$. Clearly, this sequence is an O-sequence and converges to 1. For all $n \in \mathbb{N}$, $Tx_n = 2$ and $T1 = 1$, which implies that T is not an O-continuous mapping. It is easy to check that T is an orbitally O-continuous mapping.
(B) To prove this, we consider the following cases:
Case-I: Let us consider $x \in (0, 1)$. Then

$$\begin{aligned} O_T(x) &= \{T^n x : n = 0, 1, 2, \dots\} \\ &= \left\{x, 2, \frac{1}{3}, 2, \frac{1}{3}, \dots\right\}. \end{aligned}$$

Similarly for $x > 1$,

$$O_T(x) = \left\{x, \frac{1}{3}, 2, \frac{1}{3}, 2, \dots\right\}.$$

Therefore for all $x \in (0, 1) \cup (1, \infty)$, $O_T(x)$ contains two subsequences. However, the subsequence $(y_n) = \{\frac{1}{3}\}$ is the only Cauchy O-sequence which converges in X.
Case-II: For $x = 1, O_T(x) = \{1, 1, 1, \dots\}$ contains a constant sequence which is a Cauchy O-sequence.

From the above two cases we deduce that $(X, \perp, d)$ is a T-orbitally O-complete metric space. Now we consider a sequence (x_n) in X such that $x_n = \frac{1}{n}$ for all $n \in \mathbb{N}$. Clearly, this sequence is a Cauchy O-sequence, but not convergent in X. Therefore, $(X, \perp, d)$ is not an O-complete metric space.

In the sequel, we extend the above notions in weak orthogonal metric spaces.
Definition 2.16. Let $(X, \perp, d)$ be an O_w-metric space and let T be a self-mapping on X. Then T is said to be orbitally O_w-continuous at $z \in X$ if for every O_w-sequence (y_n) in $O_T(x)$ for any $x \in X$,

$$y_n \to z \Rightarrow Ty_n \to Tz.$$

Definition 2.17. Let $(X, \perp, d)$ be an O_w-metric space and let T be a self-mapping on X. Then X is said to be T-orbitally O_w-complete if every Cauchy O_w-sequence (y_n) in $O_T(x)$ for any $x \in X$, converges in X.

3. Main results

This section comes up with the definition of generalized quasi-orthogonal contractions in a weak orthogonal metric space and it presents a fixed point result concerning such kind of maps. We also illustrate an example to validate our findings.
Definition 3.1. Let $(X, \perp, d)$ be an O_w-metric space and let T be a self-map on X. Then T is a generalized quasi $\perp$-contraction if

$$d(Tx, Ty) \leq kM(x, y)$$

holds for all orthogonally related elements $x, y \in X$, where, $0 \leq k < 1$ and

$$\begin{aligned} M(x, y) &= \max\{d(x, y), d(x, Tx), d(y, Ty), d(x, Ty), d(Tx, y), \\ &\quad d(T^2x, x), d(T^2x, Tx), d(T^2x, y), d(T^2x, Ty)\}. \end{aligned}$$

Now we discuss one fixed point result related to such kind of contractions.

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Editor speaks.....

It is high time the focus of the critics and research scholars shifted from urban/ metropolitan to rural/tribal or Adivasi literature.The forces of the urbanisation,print culture and commecialisation have resulted not only in keeping the Adivasi communities marginalised but also have adversely affected their laguages and literary cultures .Tribes in India are still thousand miles away from the mainstream of the society: the urban and metropolitan.However,it should not be pushed to oblivion that the roots of Indian literary tradition lies in the rich oral literature of the tribes/Adivasi/Banavasi.Their verses , in the form of songs or chantings are expressions of their existence and close connection with their soil and the world of nature.The folktales,songs and literature have been orally transmitted from one generation to another and survived for ages in the face of several threats like modernisation and advancement in various fields. Yes, we have achieved materialistic prosperity but on the other hand become aesthetically bankrupt to appreciate the undying beauty of the unwritten literature by making proper study.It is a pity that a large number of folktales of the tribes, in other words their rich literature are already lost due to the very fact that those are in oral forms.

Hence, attempts must be made with concerted efforts at an accelerated pace for collection and conservation of tribal languages and their rich literature that are under serious threats.We may lose an invaluable part of our history and rich literary heritage in case we fail to document the tribal history, literature that are in oral forms.

So, there is an urgent need to create a space for the study of tribal literature within the canonised written texts .Identifying and reading literature in which orality is not dissmissed as casual utterances in different dialects need to be ensured .

'Rock Pebbles' has been constantly trying to publish research works on marginal literature,Adivasi/Banabasi and other socially vulnerable people of the country.

Our heart-felt gratitude to the scholars, literature enthusiasts and well wishers for their unconditional support to make the journal a 'Rock of Gibraltar'.

- Chief Editor

■ ■

Indian Democracy: A Case Study in Political Violence and Peace Building

Saroj Kumar Sarkar

India is the largest liberal democratic country in the world. For more than seventy four years we have been witnessing the conduct of successful elections, peaceful changes of government at the Centre and in the States, people exercising freedom of expression, movement and religion. India has also been developing and transforming economically and socially. At the same time we, quite often, listen complains about prevalent inequalities, injustice or non-fulfillment of expectations of certain sections of the society. Indian democracy has been suffering so many problems as like as political violence, intolerance, poverty, illiteracy, casteism, communalism and religious fundamentalism, unemployment, corruption, criminalisation of politics. At present time , Indian democracy is passing through various crises and difficulties. Political violence and political murders are rapidly increasing at present times in India. It is dangerous threat to Indian democracy.

Keywords: Democracy, casteism, criminalization,Political murder, competitive politics.

India is the largest democratic country in the world. It is a democratic country which is mentioned in our Constitution . What is Democracy ? Meaning of Democracy long back, former President of the United States of America, Abraham Lincoln said, "Democracy is a government of the people, for the people, and by the people." [1] Today , democracy is defined as a form of government in which the supreme power is vested in the people and exercised by them directly or indirectly through a system of representation usually involving periodic free elections. Democracy has been defined in many ways. Bryce believes that "Democracy really means nothing more or less than the rule of the whole people, expressing their Sovereign will by their votes".[2] In the present age, democracy is just not limited to political democracy. It means more than a mere form of government. In its comprehensive form, democracy means, or ought to mean, (i) a form of government, (ii) a type of state, (iii) a pattern of social system, (iv) a design of economic order, and (v) a way of life and culture.[3]

Political Violence: Political violence is the deliberate use of power and force to achieve political goals.(WHO,2002). Political violence is characterized by both physical and psychological acts aimed at injuring or intimidating populations .[4] Violence has been

political violence in our country. BJP is the political branch of the RSS. The RSS declared cultural Nationalism which mean 'one nation, one state and one culture. BJP and the like minded organisations like Vishaw Hindu Parishad (VHP) , Brajrang Dal and Shiv Sena want to spread Hindu nationalism resulting in politicization of Hinduism, and national secularisation. The resultant, political violence is increasing at present times throughout India which creates problem in democratic atmosphere and damages national integrity and peace among the people.

India is a multi-party state. There are many national parties, state level parties, regional parties in India. These are created on the basis of caste, language, region and religion. Different regional parties are involved in competitive vote bank politics. They want to capture political power. In this way they are involved in conflict and create violence.

Political violence is correlated with Political criminalization**.** In recent years, criminalization of politics in India has become a debatable issue. There have been allegations that there are some elements in politics that do not have faith on democratic values and practices. They indulge in violence and take refuge in other unhealthy, undemocratic methods to win elections. Undoubtedly, this is not a healthy trend in politics and there is an urgent need to apply serious check on such tendencies. Criminalization of politics is the very negation of democratic values and has no place in a democratic set up. Democracy can be strengthened by adopting and promoting democratic values and shunning criminal activities. Recently, the judiciary, while taking a serious note of criminal tendencies in politics, has showed signs of adopting remedial measures to apply a serious check on such elements. The Central government and many State governments have been taking steps to address this issue effectively. This is a matter of great satisfaction and a healthy sign for the successful functioning of democracy in our country. We, as awakened citizens and as voters of the largest democracy in the world, can also contribute by discouraging such persons who have a criminal background, from contesting elections. We find some unfair means like booth capturing, vote ragging, threatening the voter by the party muscleman or *goonda* in election period. The general voters are failed to vote as per their own choice. It is a very bad culture in our country which is increasing day by day.

Unemployment is also related with political violence. Educated unemployed men join with different political parties with a hope to earn. They take it as a source of income, so we find group conflict in a party which creates violence among them. Party members and cadres want to grip the power which moved the competition and conflict.

Casualties: The victims in these clashes are mostly innocent people like students, teachers, labourers, farmers, agricultural workers and small shopkeepers. Most affected people in West Bengal pre and post poll violence are from *Dalit* community[15].

Political violence is implicated in a range of mental health outcomes, including depression and anxiety. It is a great threat to the democratic values and peaceful situation in

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A CRITICAL STUDY ON THE CORRUPTION IN INDIA AND ITS REMEDIES.

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Abstract: Corruption in India is an issue which affects the economy of central, state and local government agencies in many ways. Corruption is a great problem in India. It is not only Indian problem but also world wide problem. We have found it every countries less or more. India is largest democratic country in the world. It has long history of financial, Political, Administrative corruption. After independence, we have noticed many corruption and Financial scam which were done by political leader or Ministers, and bureaucat in our conntry. It has spread top to bottom in nation. It is a great challenge to remove from our administration. People are losing their faith on administration, judiciary system, and political leaders. Social morals and values are spoiling day by day. It has so many causes as like as Political patronge, nepotism, greediness, lack of transparency, increasing of unemployment, low wage of government officials, etc. It badly affected our society. Our country has taken so many measure to prevent it but fail to cure this disease at all.

Keywords: Corruption, Political patronge, Greediness, Nepotism, Democratic.

Introduction:

Corruption in public life has been a major concern in India. In 2019, India was ranked 80th of 180 countries defined as corrupt in Transparency International's Corruption Perceptions Index (CPI). India fell to 85 rank in **Corruption** Perceptions Index in 2021.[1] In fact, corruption is rampant in all walks of life, be it land and property, health, education, commerce and industry, agriculture, transport, police, armed forces, even religious institutions or socalled places of spiritual pursuits. Corruption continues to exist in covert and overt ways at all three levels - political, bureaucratic and corporate sector. One can see the nexus between the politicians, the bureaucrats and the industrialists which has resulted into corruption and corrupt practices. The tentacles of corruption have affected all organs of government, including the judiciary. India is corrupted democracy; corruption is found from top to bottom. Decentralisation of power is a main

are given prominent positions like members of parliament or even higher posts. Instead of being disrespected, they are respected.

8. Lack of Public Unity: The public openly criticizes corruption, but interestingly there is no unity among the public to stop corruption. If a person wants to get his done his work, he gets it done by corruption means if possible and then later criticizes the corrupt official. If the public stands united against corruption so that no one is ready to offer bribes to get their work done, then the corrupt officials will have no other option but to work in a corruption-free manner. During the election, politicians try to lure the people by offering money and other things. If these politicians win and get power, they try to regain 10 to 100 times the amount spent in the process.[4]

9. Lack of transparency in affairs and deals: Many seat selection processes like in education, contracts for the job, employee income reports (wealth possession), etc., lack transparency.

10. Lack of Independent detective agency: Lack of an independent detective agency to investigate with full power and freedom to expose the corrupt individuals. The existing agencies are under the control of either the government or the armies and are not free to work. Hence anyone who commits offense will not be afraid of the investigation as they can escape from it by taking the help of those controlling them.

11. Lack of state funding for elections: State funding for polls is the best way to beat corruption. Political parties receive party donations and will not disclose them to the fullest. In doing so, they encourage corruption.

They collect massive amounts from industrialists with a promise to help when in power. The presence of state funding can abolish party donations and minimize corruption.

12. The option of many political parties: In a democracy, anyone can establish a political party. So there are chances for the corruption of many political parties in the country.

If a political party wins, then the party members will desire to expand the party all over the country. To do so, they need enough financial reserves. Once they come into power, they opt for corrupt means to make the wealth needed to expand the party.

13. Lack of enough powers to the judicial system: and other independent organizations. Like the election commission cannot ban a politician from contesting in case they make a mistake or do not comply with the rules during the poll campaign (like distributing money to people etc.). Similarly, **the judicial system has low options to punish someone who is found to be**

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The impact of MOFs in pH-dependent drug delivery systems: progress in the last decade

Diptiman De and Prithidipa Sahoo *

Metal–organic frameworks (MOFs) are porous crystalline materials consisting of one-, two-, or three-dimensional networks created by metal ions/clusters and multidentate organic linkers through coordination bonding. MOFs are one of the most favorable candidates for biological applications such as wound dressings, cardiac prosthesis, tissue engineering, bioimaging, and drug delivery and as cancer theranostic systems due to their high surface area and porosity for the high loading of therapeutic agents and facile modification of their physical (*e.g.*, pore size and shape) and chemical properties. Drug delivery involves the administration of drugs using a suitable carrier for achieving treatment without unwanted side effects. In the last few years, several types of MOFs have been synthesized including Zn-based MOFs, MIL series MOFs, and Zr-based MOFs and evaluated for their use in different biomedical fields, especially drug delivery. After Fe, zinc is the second most available element in the body, and hence Zn-based MOFs can be considered enduring platforms for various biomedical uses, especially drug delivery applications. MIL series composites and Zr-based biomaterials are also suggested for several biomedical applications due to their good mechanical properties, biocompatibility, and bioactivity. This review highlights the different types of Zn-based and MIL series MOFs that have been used as suitable pH-responsive drug delivery systems and summarizes the Zr-based MOFs that have been used as suitable pH-responsive or reverse pH-responsive drug delivery systems and also discuss their drug-releasing phenomenon at different pH ranges.

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Introduction

Metal–organic frameworks, abbreviated as MOFs, represent a new class of periodic, crystalline, and highly porous (up to 94% space) materials. Generally, MOFs are formed by the linkage of inorganic metal (*e.g.*, transition metal and lanthanide metal) ions/clusters as the node with organic ligands (*e.g.*, carboxylates, phosphonates, imidazolates, and phenolates), which are called linkers, exhibiting high porosity and thermal stability (Fig. 1).[1] Various common ligands are used in the synthesis of MOFs, as presented in Fig. 2. In the past two decades, metal–organic frameworks (MOFs) have been shown to possess conventional properties such as different pore shapes, desirable pore size, large surface areas, and the ability to encapsulate compounds and drugs.[2] In 1965, the journey of the metal–organic framework started with the synthesis of thermally stable Zn coordination polymers.[3] Thereafter, in 1990, the research group of Hoskins and Robson proposed scaffold-like 3D frameworks.[4] In 1995, Yaghi and co-workers designed the selective binding and removal of guest molecules in a microporous MOF composed of 1,3,5-benzenetricarboxylate (BTC) and cobalt cation,[5] while the same group reported the design and synthesis of MOF-5 in 1999.[6] MOF-5 contains 1,4-benzenedicarboxylate (BDC) and Zn_4O clusters and shows an exceptionally high Langmuir surface area of 2900 $m^2\ g^{-1}$. A brief history of metal–organic frameworks is schematically represented in Scheme 1. Presently, researchers are focused on exploring different types of luminescent MOFs for the development of advanced practical applications.[7] Metal–organic-framework (MOF) materials are increasingly gaining interest in various applications such as gas storage and separation,[8] chemical separation,[9] catalysis,[10] sensing,[11] semiconductors,[12] magnetism,[13] and bioimaging[14] (Scheme 1). During the past

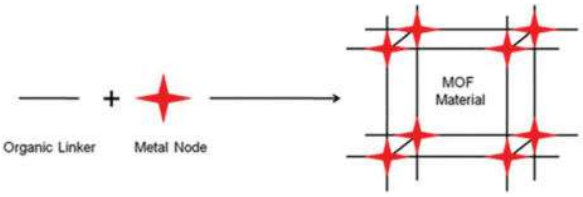

Fig. 1 Basic structure of a metal–organic framework (MOF).

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methods, the total specific surface area and pore volume of the Ins-GOx/ZIF-8 hybrid composites were shown to be 1219 m^2 g^{-1} and 0.501 cm^3 g^{-1}, which were lower than that of pure ZIF-8 (1449 m^2 g^{-1} and 0.646 cm^3 g^{-1}), respectively. The protein-embedded ZIF-8 appeared to be able to respond to a decrease in surface area and average pore size. The insulin release profile of Ins-GOx/ZIF-8 at different glucose concentrations was studied to analyze the glucose response features of Ins-GOx/ZIF-8. At the hyperglycemic level, a rapid insulin release rate (roughly 420 g mL^{-1}) was found after 4 h. At 24 h, about 84 and 145 g mL^{-1} of loaded insulin were released at the control and normoglycemic levels, respectively. When a high quantity of glucose was detected, a large amount of glucose entered the pore of the composites and contacted GOx, causing glucose to be oxidized to gluconic acid and H_2O_2. The decrease in pH facilitated the release of insulin stored in ZIF-8 to achieve the goal of lowering the blood glucose level (Fig. 8). The MTT assay on HeLa cells confirmed that the biocomposite had very low cytotoxicity, having good biocompatibility. Consequently, it could be utilised for subcutaneous insulin injections, minimizing the need for frequent glucose monitoring and multiple injections.

Interestingly, Qu and co-workers reported an aAuNCs-MOF as a viable option in cancer therapy due to its unique properties of increased luminescence, negligible cytotoxicity, dramatic pH-dependent luminescence, and the ability to encapsulate hydrophobic drugs.[58] $Zn(NO_3)_2{\cdot}6H_2O$, aAuNCs, and 2-methyl imidazole methanol solution were used to prepare aAuNCs-MOF. Given that the aAuNCs aggregate in methanol with enhanced luminescence and ZIF-8 could be produced in methanol, ZIF-8 was a good choice for encapsulating aAuNCs among the various MOFs. According to this study, aAuNCs-MOF exhibited a rhombic dodecahedron shape, which was consistent with that of pure ZIF-8. Type I isotherms were observed for aAuNCs-MOF with a surface area of around 1674 m^2 g^{-1} and an average micropore diameter of 0.99 nm. The decrease in the gravimetric Brunauer–Emmett–Teller (BET) surface area of AuNCs-MOF compared to pure ZIF-8 (1745 m^2 g^{-1}, 1.20 nm) indicated the encapsulation of nonporous AuNCs in MOF. The hydrophobic drug camptothecin (CPT) was chosen as the guest molecule in the controlled release study. The loading efficiency of CPT in aAuNCs-MOF was 9.4%. Given that ZIF-8 was stable in neutral and alkaline aqueous solution but quickly degraded in acid solution, the drug release rate from aAuNCs-MOF was substantially faster at pH 5.0 and pH 6.0 than at pH 7.4. The green fluorescence from fluorescein in CPT became stronger as the incubation time increased from 4 to 24 h, whereas the luminescence of AuNCs became weaker, indicating that the fluorescein molecules and AuNCs were released from aAuNCs-MOF due to the degradation of the MOF in the endo/lysosomes (pH 5–6). Consequently, aAuNCs-MOF could track the release of hydrophobic drugs in real time (Fig. 9). CPT@aAuNCs-MOF had better cytotoxic efficacy than free CPT, indicating that aAuNCs-MOF is a potential platform for delivering medicines to cancer cells. This phenomenon has led to the development of new luminescent drug delivery systems to increase opportunities for biological and medical applications.

Nowadays, motile metal–organic frameworks are used as small-scale robotic platforms for applications such as environmental remediation, targeted medication delivery, and nanosurgery. In 2019, Luis and co-workers showed novel motile RhB@ZIF-8@ABFs that could transport therapeutic payloads to a designated location within a cell culture to demonstrate their targeted drug delivery capabilities in a biologically relevant medium. The group successfully manufactured magnetic helical microstructures coated with a zinc-based MOF, zeolitic imidazole framework-8 (ZIF-8) and assessed their biocompatibility and pH-responsive properties.[59] They made helical swimmers, commonly known as artificial bacterial flagella (ABF), with 2PP and coated them with nickel, and sub-

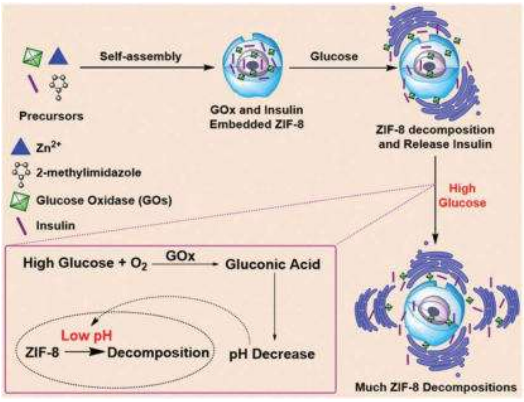

Fig. 8 Representation of glucose-triggered insulin release from the MOF-based nanosystem.

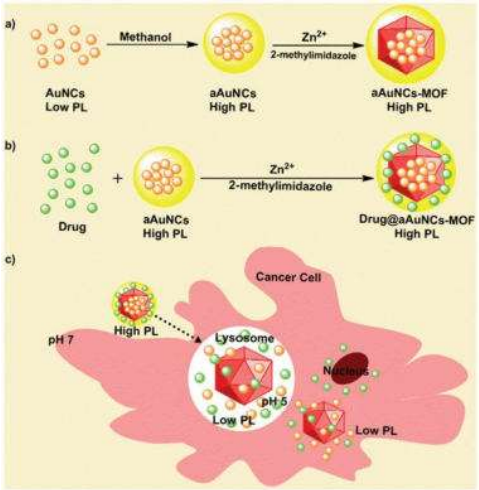

Fig. 9 (a) Representation of encapsulation of aggregated AuNCs in metal–organic framework to enhance their luminescent efficiency. (b) Encapsulation of in aAuNCs-MOF. (c) aAuNCs-MOF served as a tracking agent for the real-time imaging of hydrophobic drug release.

efficiently. In a series of PBS of pH 7.4, 6.5, and 5.5 over 168 h, the cumulative release profiles of Van from MOF-53(Fe)@Van (0.8 mg mL^{-1}) and Fe^{3+} from MOF-53@Van NPs (100 g L^{-1}) were studied. The degradation degree of MOF-53(Fe) in PBS at pH 7.4 was 0.75% and 0.17% at pH 5.5, demonstrating the high stability of the system (Fig. 13). The release amount of Fe^{3+} increased according to the increase in pH value, which indicated that the MOF-53(Fe) NPs were more stable under acidic settings than under neutral conditions. This result was in agreement with the amount of Van released at the various pH levels. With the partial breakdown of MOF-53(Fe), the rate of Van release was enhanced. Specifically, because the MOF-53 (Fe) NPs decomposed partially in neutral conditions, the amount of Van released may have a larger burst effect. IN contrast, the MOF-53(Fe) NPs degraded slower under acidic conditions (pH 5.5) and Van was released more slowly. This finding can aid in the treatment of bacterial infections in acidic environments. The antibacterial activities of Van-loading MOF-53(Fe) were investigated using the spread plate method, and the results revealed that Van-loading MOF-53(Fe) has a long-lasting antibacterial impact and high antibacterial effectiveness without cytotoxicity.

Sadr and co-workers prepared a novel magnetic and pH-responsive porous nanocomposite *via* the surface grafting of β-cyclodextrin on Fe_3O_4@Silica@MIL-100 (Fe) in 2018.[65] The fabrication of the Fe_3O_4@Silica@MIL-100 (Fe)/-CD nanocomposite as a magnetic and pH-responsive drug delivery vehicle was described in this research study. Using cephalexin as a drug model, the smart behaviour of the nanocomposite in drug loading and release was thoroughly explored. The TEM images of the Fe_3O_4@Silica NPs revealed that they possessed a diameter of less than 50 nm, making them appropriate for drug delivery applications. The ability of Fe_3O_4@Silica@MIL-100 (Fe)/-CD as a pH-responsive drug delivery system was investigated using cephalexin as a drug model. The cephalexin release behaviour was studied using buffer solutions with pH values of 1.2, 5, and 7.4. The adsorbent decomposed at a severe pH of 1.2, resulting in a robust release. At lower pH, the weak π–π interaction between the drug and adsorbent led to a greater burst effect. The stability of the drug/-CD system was higher at physiological pH 7.4 than at pH 5. They discovered that the release was greater and faster at pH 5 than at pH 7. The adsorbent demonstrated considerable release and approximately 96%, 88%, and 99% of the drug was released in 50 h at pH 5, 7.4, and 1.2, respectively. Astonishingly, at pH 5, 7.4, and1.2 around 69%, 99%, and 55% of the medication was released, respectively in 8 h. It was also determined that the percentage of drug release increased with an increase in temperature. Finally, this research presented an efficient method for producing magnetic and smart sorbents that were inexpensive and performed well in drug delivery systems for a wide range of drugs.

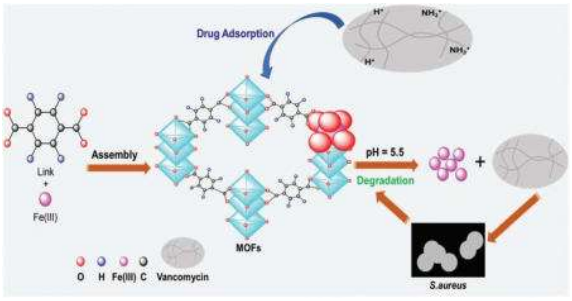

Fig. 13 Representation of MOF-53(Fe) structure and the process of MOF packing drug molecules for killing bacteria.

Yang and co-workers developed a new type of porphyrin–iron metal–organic framework (Fe-MOF) nanocrystals in 2022 as an acid-degradable drug carrier and hydrogen donor by coordinating porphyrin and zero-valence Fe atoms.[66] The $FeCl_3$-MOF nanocrystals were prepared by combining $FeCl_3$ with 5,10,15,20-tetrakis(4-pyridyl)-21*H*,23*H*-porphine (TPyP), and then reducing them with sodium borohydride. The chlorine atoms were removed during the reduction, generating homogeneously dispersed zero-valence Fe atoms. Small-angle X-ray scattering (SAXS) suggested their outstanding structural stability, which favored steady drug delivery. Doxorubicin (DOX) was encapsulated in Fe-MOF in this investigation. After loading DOX, the specific surface area and pore volume of Fe-MOF nanocrystals were reduced from 117 m^2 g^{-1} and 0.35 cm^3 g^{-1} to 103.8 m^2 g^{-1} and 0.25 cm^3 g^{-1}, respectively. The decrease in the pore volume and specific surface area of the Fe-MOF nanocrystals (DOX@Fe-MOF) suggested that DOX was successfully loaded in their pore channels. Because of the microporous nature of Fe-MOF and the hydrogen interactions between the pyridyl groups of Fe-MOF and amino/hydroxyl groups of DOX, the DOX loading capacity of Fe-MOF was measured to be as high as 940 mg g^{-1}. In the acidic PBS environment, the Fe-MOF nanocrystals disassembled rapidly into free ions. Consequently, both hydrogen gas and the loaded medication DOX were produced in an acid-responsive manner. In pH 7.4 PBS, the Fe-MOF nanocrystals appeared to degrade slowly due to the high activity of the single-atom Fe (0). However, it was worth mentioning that Fe-MOF nanocrystals could remain stable for the first hour without observable degradation, hydrogen generation, or drug leakage. Notably, rapid drug release in the acidic environment of the tumor (pH = 6.5) favored tumor cell death, while slow drug release in normal tissues (pH = 7.4) avoided acute drug toxicity to normal cells/tissues and hydrogen gas not only enhanced the anticancer effects of the chemotherapeutic drugs but also reduced their toxic side effects and drug leakage (Fig. 14). The released hydrogen gas from the nanomedicine effectively sensitized the chemotherapy of MCF-7/ADR cells by down-regulating the expression of P-gp and decreasing the ATP levels, resulting in increased ROS-mediated DNA damage, which aided DOX in effectively inhibiting metastasis by immuno-activating M1 macrophages and suppressing MMP-2 expression. The good flexible Fe-MOF platform favored both high anti-MDR and anti-metastasis outcomes and high bio-safety of the

the impacts of exposure to numerous substances in their environment, such as moisture, solvents, acids, bases, and aqueous solutions containing coordinating anions. The capacity of MOFs to maintain their structural integrity when exposed to heat, vacuum, or pressure is frequently correlated with their thermal and mechanical stability. Over the last two decades, significant effort has been devoted the *de novo* synthesis of novel MOFs with high stability using various strategies, such as preparing high-valent metal–carboxylate or low-valent metal-azolate MOFs using azole-containing carboxylate linkers, mixed metal ions, and hydrophobic ligands, insertion of building blocks, and framework interpenetration. To improve the stability of existing MOFs, post-synthetic structural processing and composite material engineering have also been applied. Although much progress has been made in this field, there are still many obstacles to be overcome. It is difficult to find a universal technique that can be applied to diverse MOF systems due to the specific requirements of each strategy. In addition, many pre- or post-synthetic alteration procedures vary the pore characteristics of MOFs, which complicates their further applications. Some specific techniques, such as hydrophobic surface treatment may be worth further exploration to solve these concerns. Experiments can also be rationally integrated with computational design to produce new framework materials with great stability and specific features. These investigations can be used to explore the biomedical (*e.g.*, drug delivery and bio-imaging) use of nontoxic MOFs. Nontoxic MOFs can be investigated for application as strong supports for regular bioactive atoms to expand their timeframe of realistic usability and adequacy. Furthermore, MOFs should be assessed for their antibacterial and antifungal activity to examine their clinical and natural applications. Despite numerous outstanding studies, the research on MOF toxicity and biodegradation is still in its infancy. Before using these nanocomposites in the clinical setting, numerous hurdles must be overcome. Firstly, greater effort should be devoted to fabricating adaptable nontoxic or low-toxicity MOFs, which should also be biocompatible to accomplish prolonged blood circulation and ensure that the decomposition products can be digested by the body's metabolic system. To minimize adverse effects, future research should focus on constructing non-toxic MOF carriers using endogenous building blocks or functionalizing MOFs with bioactive molecules. Furthermore, thorough *in vitro* studies of the stability and degradation mechanisms of MOF-based nanocarriers are required and also systematic *in vivo* investigations are essential to optimize the performance of MOFs before their clinical applications. To highlight a key point, studying the therapeutic effects of nanocarriers and their effects on normal organs is insufficient. Additional efforts must be made to understand the metabolic mechanisms and pathways of nanocarriers in *in vivo* systems, and long-term monitoring of the organism is also necessary. Finally, future work should be concentrated on the development of multimodal MOF-based theranostic platforms with various mechanisms to achieve high anticancer efficacy and treatment of other disorders. Scientists have made great advancements in developing theranostic MOFs for clinical applications, even though theranostic MOFs are still a long-standing challenge in nanomedical research. Nevertheless, it is believed that promising advances in MOFs for clinical use will be made in the near future. The fabrication of very stable MOFs is likely to remain a dream, but it would pave the way for their use in a variety of applications. For instance, stable and well-designed multivariate MOFs or MOF-based materials with the characteristics of each portion can provide exceptional performances for certain applications. Moreover, by using stepwise synthetic approaches to control the precise position of customizable functional groups within stable MOFs, their considerable potential or optimal performance for a variety of applications will be understood. The analysis of the mechanism for device engineering and applications is a probable fascinating aim to achieve stable MOFs in the future.

Author contributions

D. D. searched all the articles, interpreted data and prepared the manuscript. P. S. conceptualized the review, wrote and edited the manuscript.

Conflicts of interest

There are no conflicts to declare.

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