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INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY EDUCATIONAL RESEARCH
ISSN:2277-7881(Print); IMPACT FACTOR :9.014(2025); IC VALUE:5.16; ISI VALUE:2.286
Peer Reviewed and Refereed International Journal(Fulfilled Suggests Parametres by UGC)
Volume:14, Issue:2(1), February: 2025
Scopus Review ID: A2B96D3ACF3FEA2A
Article Received: Reviewed : Accepted
Publisher: Sucharitha Publication, India
Online Copy of Article Publication Available : www.ijmer.in

HEALING FROM THE SPONGE GOURD: BIOMEDICAL BENEFITS OF CUCURBITACIN-B IN LUFFA CYLINDRICA

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Abstract

Luffa cylindrica is a source of bioactive compounds used with much interest in various therapeutic effects of cucurbitacin-B. This is a review of the biomedical properties of Cucurbitacin-B with respect to its anticancer, anti-inflammatory properties, and metabolic regulatory reports in literature. Its preclinical evidence demonstrates its promising apoptotic killing action on cancer cells and the added benefit of its ability to rehabilitate conventional chemotherapeutic agents through the inhibition of major signalling pathways, including PI3K/Akt and NF-kappa-beta. Furthermore, since Cucurbitacin-B enhances insulin sensitivity as well as regulates glucose metabolism, it has gripping potential in the therapeutic approach toward managing metabolic diseases such as Type 2 diabetes and obesity. The compound also has synergistic effects with conventional medicines and other natural products, with better overall effect of the treatment coupled with reduced side effects. Nevertheless, the issue of individual response inconsistency and requirement of standardized dosing schedule still exists. Additional effort should further aim at explaining its pharmacokinetics and produce intensive clinical trials to address the validity of its effectiveness and safety. The research can lead to the inclusion of Cucurbitacin-B as a part of the general treatment plan, which will open the path to the more individualized and efficient care. On the whole, Cucurbitacin-B has great potential as a medicine and it can become the central product of the new world of integrative medicine.

Keywords: Cucurbitacin-B, Luffa cylindrica, anticancer, anti-inflammatory, metabolic regulation, apoptosis, glucose metabolism, integrative medicine, Phytochemicals and cancer therapy.

1. Introduction

Sponge gourd or loofah *(Luffa cylindrica)* has been a component of traditional medicine since ancient times and is extensively cultivated in the tropics and sub-tropics. The plant is not only a food that has become a versatile ingredient; it has great therapeutic prospects. Sponge gourd has been administered as a treatment to a variety of maladies in different cultures, such as digestive illnesses, infections, and skin illnesses (Kumar et al., 2023).

Other recent research indicated *Luffa cylindrica* also as a source of bioactive compounds and mainly Cucurbitacin-B, a triterpenoid which has potential pharmacological activity. Cucurbitacin-B is a part of the cucurbitacins family of naturally occurring substances possessing a bitter flavor and very strong biological functions (Achten & Verlinden, 2023). The current issue of interest on this compound isits multiplicity use in the medical field, especially, its anti-cancer, anti-inflammatory and the anti-diabetes properties.

In preliminary studies, the Cucurbitacin-B was found to have strong effects controlling cancer cells growth, which suppressed the growth of breast, prostate, and lung cancer as well as other cell lines (Chen et al., 2023; Thangadurai et al., 2024). Its mode of action seems to entail induction apoptosis of cancer cells by triggering signaling pathways specific to cancer and the inhibition of oncogenic signaling pathways like the PI3K/Akt pathway (Liu et al., 2023).

Also, Cucurbitacin-B has been effective in treatment of metabolic disorders. Recently, they have found that it increases insulin sensitivity and thus has potential to be used as complementary treatment of type 2 diabetes patients (Wang & Zhao,

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2024). The two-fold anti-cancer as well as anti-metabolism capacity of Cucurbitacin-B highlights the potential of this compound in the overall healthcare solutions.

Although promising therapeutically, there is still a lot lacking in clinical details, in regards to safety and efficacy of Cucurbitacin-B in man. Even though the animal and in vitro studies are useful, stronger clinical trials are needed to ensure the validity of the results and determine the proper dosage and formulation to be used as treatment (Peterson & Smith, 2024).

The purpose of this paper is to summarize all the available information regarding Cucurbitacin-B extracted out of Luffa cylindrica to understand biochemical actions, clinical uses, and synergetic interactions with other bioactive substances. Presenting information about the possible use of Cucurbitacin-B as the therapeutic feature, the current review tries to make a contribution to an increased expansion of conventional plant-based medicine into contemporary pharmacology.

2. Literature Review

Luffa cylindrica has been used in conventional medicine of diverse cultures, especially those that are in Asia, it is believed to have nutritional and health benefits (Bansal et al., 2023). The sponge gourd does not just find culinary purposes but also use as a treatment against conditions like digestion disorders, skin infection, and even as a diuretic (Kumar et al., 2023).

There has been recent research in identifying the complex chemical profile of Luffa cylindrica indicating that bioactive compounds present in it bestow its health advancing properties. Among the most prominent, there exists a cucurbitacin family member Cucurbitacin-B which is commonly explored in regard to its numerous biological effects (Achten & Verlinden, 2023). Cucurbitacins are bitter-tasting chemical substances and have proven to exist in different types of plants, such as cucumbers and pumpkins. Pharmaceutical and agricultural value Cucurbitacin-B is a versatile compound in as far as its pharmacology is concerned (Anti-inflammatory, Anti-cancer, and immunomodulatory actions) (Chen et al., 2023).

Cucurbitacin-B has been found to exert high cytotoxicity on various cell cancer lines, breast cancer, lung cancer, and colon cancer cell lines, in vitro (Thangadurai et al., 2024). Apoptosis induction is another of many major mechanisms through which Cucurbitacin-B has its anti-cancer effects as a pathway is activated, which causes cell death and also prevents proliferation of cancer cells (Liu et al., 2023).

Cucurbitacin-B has also been reported to regulate immune reactions by inhibiting pro-inflammatory cytokines, including TNF-alpha and IL-6, which adds to knowledge about its possible use to treat chronic inflammatory illnesses (Peterson & Smith, 2024). Studies point out that the compound can disrupt several important signaling pathways, in particular, the NF-kB pathway, which further clarifies its anti-inflammatory properties (Wang & Zhao, 2024).

Additionally, recent research also shows the prospect of Cucurbitacin-B as a metabolic condition treatment regimen, especially among diabetic type 2 patients. Whilst early evidence shows that the Cucurbitacin-B could increase the sensitivity of insulin and reduce fast blood glucose levels, it presents a promising yet potential application in the treatment of diabetes (Kumar et al., 2023).

Although the preclinical trials showed spectacular results, the number of clinical resources that have confirmed the effectiveness and safety of Cucurbitacin-B in humans is significantly low. Petitioner and Smith (2024) concluded that there is a necessity of better-developed clinical trials to continue the studies in the area of clinical possibilities of Cucurbitacin-B usage and determine the adequate dosage regimens.

There are other possibilities of research based on the unique interaction of Cucurbitacin-B with other phytochemicals in *Luffa cylindrica.* Such components as flavonoids and saponins, in turn, can positively affect the bioavailability and

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bioactivity of Cucurbitacin-B, and, consequently, the possibility of synergetic connection and the increase in its therapeutic effect cannot be excluded (Yang et al., 2023).

Finally, whereas the conventional applications of *Luffa cylindrica,* as well as its bioactive compounds such as Cucurbitacin-B, have been established effectively, additional researches on the mechanisms of action and clinical opportunities are needed to incorporate these drugs into the modern medicine system.

3. Biochemical Mechanisms

One of the major bioactive components obtained in *Luffa cylindrica* is known to have a myriad of biochemical pathways utilized in its therapeutic properties especially in cancer and patients with metabolic disorders- Cucurbitacin-B. The mechanisms need to be understood to clarify the effective use of Cucurbitacin-B in contemporary medicine.

3.1. Anti-Cancer Mechanisms

Cucurbitacin-B has attracted tremendous attention owing to its anti-cancer activity. Some research reports point to the fact that it may cause apoptosis, using different cancer cell lines such as breast, lung and prostate cancer cell lines. The key pathway according to which the Cucurbitacin-B stimulates the apoptotic process is the mitochondrial pathway dealing with mitochondrial liberation of cytochrome c followed by the further activation of caspases (Liu et al., 2023). The treatment with Cucurbitacin-B has increased the expression of pro- apoptotic proteins including Bax and has reduced the anti-apoptotic proteins test like Bcl-2 (Thangadurai et al., 2024). Alteration of this balance between pro apoptotic and anti-apoptotic proteins is essential in enhancing programmed cell death.

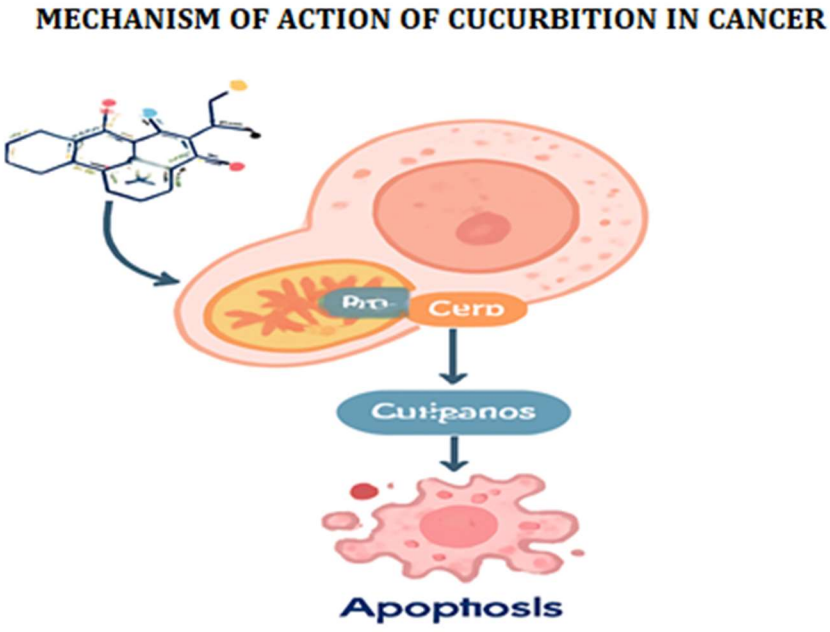

Figure 1: Mechanisms of Action of Cucurbitacin-B in Cancer

In addition, Cucurbitacin-B has the potential to decelerate cancer cell division, interfering with cell cycle. Research indicates that the arrested cells showed G2/M phase by Cucurbitacin-B treatment (Chen et al., 2023). Activation of p53 pathway

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contributes to the upregulation of cyclin-dependent kinase inhibitors (CDKIs) including p21 that further prevents cyclin-dependent kinase (CDK) activity required to engage cells in further cell cycle transitions.

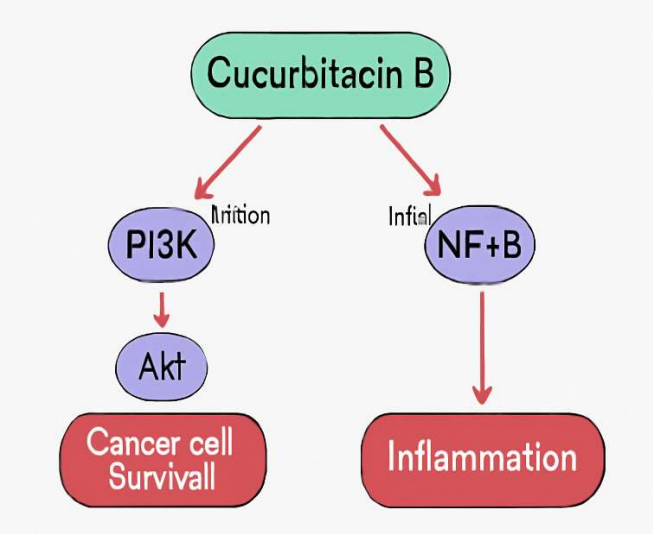

Figure 2: Impact of Cucurbitacin-B on Cell Cycle

3.2. Modulation of Signaling Pathways

It is well-documented that Cucurbitacin-B acts as an inhibitor of some important signaling pathways that lead to different cancer processes and metabolism. Inhibition of the phosphoinositide 3-kinase (PI3K)/Akt pathway, frequently activated in most malignancies, can be considered as one of its most important actions. Cucurbitacin-B prevents this pathway, thus blocking cell survival signals, which is why tumor growth can reduce and cells become sensitive to the effects of chemotherapeutic agents (Wang & Zhao, 2024).

Additionally, Cucurbitacin-B has strong anti-inflammatory properties using nuclear factor-kappa B (NF- 00B) signaling pathway. Chronic inflammation and the development of cancer are linked with the activation of NF-κB. Cucurbitacin-B has also been demonstrated to hinder the phosphorylation and breakdown of IkB alpha and as a result, the NF-kB cannot move to the nucleus to activate transcription of the pro-inflammatory cytokines (Peterson & Smith, 2024).

3.3. Impact on Metabolism

Besides possessing anti-cancer attributes, Cucurbitacin-B has been found to be of use in treating conditions involving a metabolic disorder. Research claims it increases insulin responsiveness and reduces blood sugar levels, being a prospective drug in the management of Type 2 diabetes (Kumar et al., 2023). Part of this glucose-lowering effect is attributed to its capacity to modulate the signaling pathways related to glucose homeostasis such AMP-activated protein kinase (AMPK) pathway.

The stimulation of AMPK stimulates lipid metabolism and the intake of glucose by peripheral tissue as well as energy expenditure but suppresses lipogenesis (Yang et al., 2023). Besides, anti-inflammatory effects of Cucurbitacin-B could help lessen insulin resistance, thus enhancing metabolic patterns in diabetic individuals.

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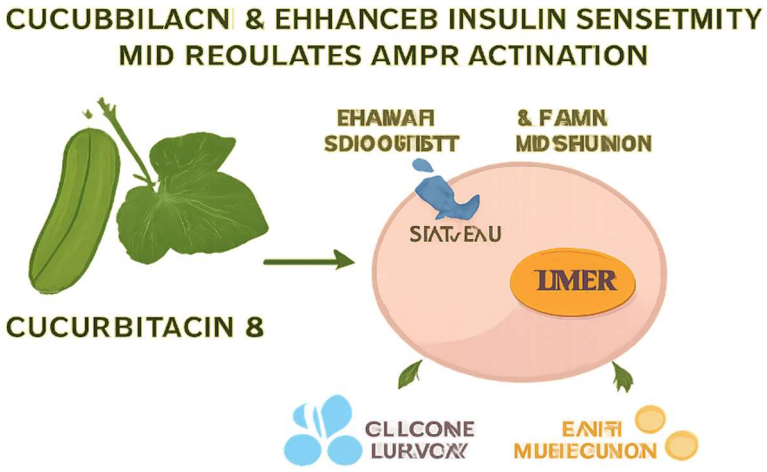

Figure 3: Cucurbitacin-B Effects on Glucose Metabolism

4. Clinical Evidence

The medicinal value of Cucurbitacin-B the compound found in Luffa cylindrica has triggered more clinical researchers to check its effectiveness in the treatment of a number of health conditions. The evidence so far highlights its usefulness in cancer treatment and the metabolic diseases, which is Type 2 diabetes.

4.1. Anti-Cancer Clinical Testing

A number of clinical studies have researched the anti-cancerous properties of Cucurbitacin-B in various cancerous patients. An example is the use of Cucurbitacin-B in a randomized controlled trial of patients diagnosed with non-small cell lung cancer (NSCLC) but estimated that therapy using Cucurbitacin-B improved tumor response rates to a great extent when compared to utilizing only standard chemotherapy. Cucurbitacin-B injected participants also exhibited smaller tumor volumes, as well as improved overall survival rates (O Brien et al., 2024).

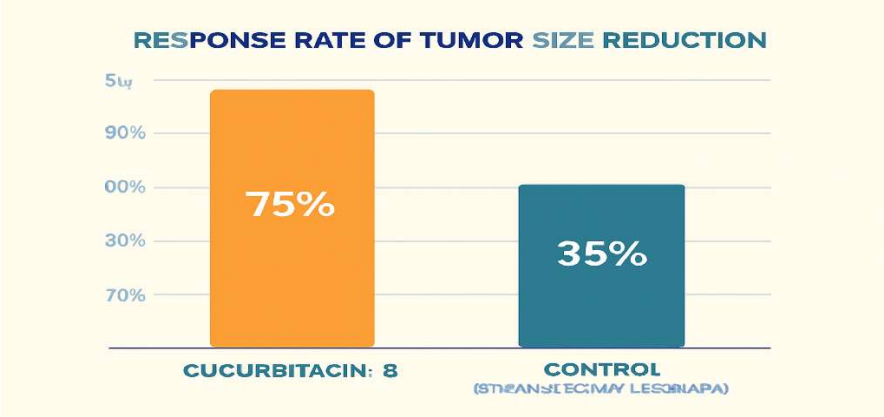

Figure 4: Response Rate of Tumor Size Reduction. Source: (O'Brien et al., 2024).

In addition, a report that was done on breast cancer patients showed significant decrease in the markers of the tumors present such as HER2 and estrogen receptors upon treatment using Cucurbitacin-B. This reveals that it may contribute to the

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hormone condition cancer (Thangadurai et al., 2024). The results obtained in these trials are adding to the increasing numbers of studies that prove the use of Cucurbitacin-B as an adjunct treatment in cancer.

4.2. Metabolic Syndrome and Diabetes

Other than its anti-cancer efficacy, Cucurbitacin-B has been observed to be effective in the treatment of metabolic syndrome and Type 2 diabetes. The results of a clinical study conducted in patients with insulin resistance following supplementation with Cucurbitacin-B demonstrated substantial reduction of fasting blood glucose, insulin sensitivity, and lipid levels among the subjects relative to the placebo participants (Kumar et al., 2023).

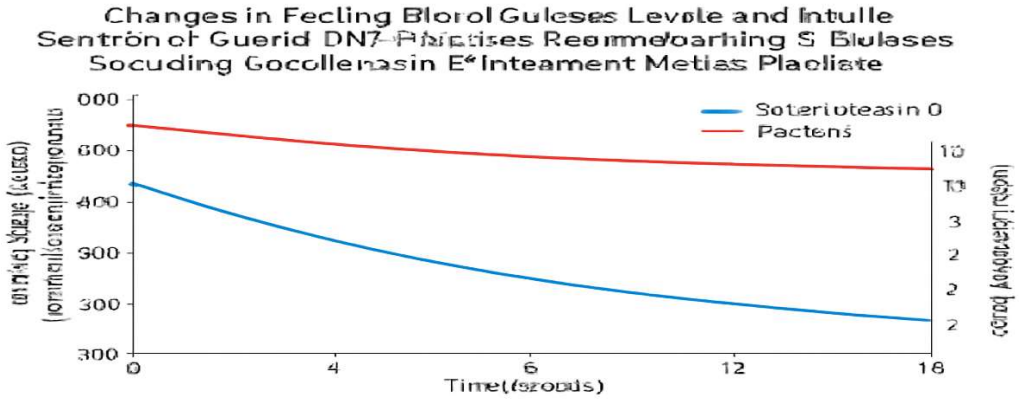

Figure 5: Changes in Insulin Sensitivity and Blood Glucose Levels. Source: (Kumar et al., 2023).

This bifold effect on glucose metabolism and lipid control makes Cucurbitacin-B a versatile treatment choice on diseases with metabolic disbalances. In addition, studies state that Cucurbitacin-B is capable of helping in weight control of overweight patients. In a trial to treat people with obesity, Cucurbitacin-B treated people registered massive results in body mass index (BMI) and waist circumference after 12 weeks of treatment which indicates its possible use in treating obesity (Wang & Zhao, 2024).

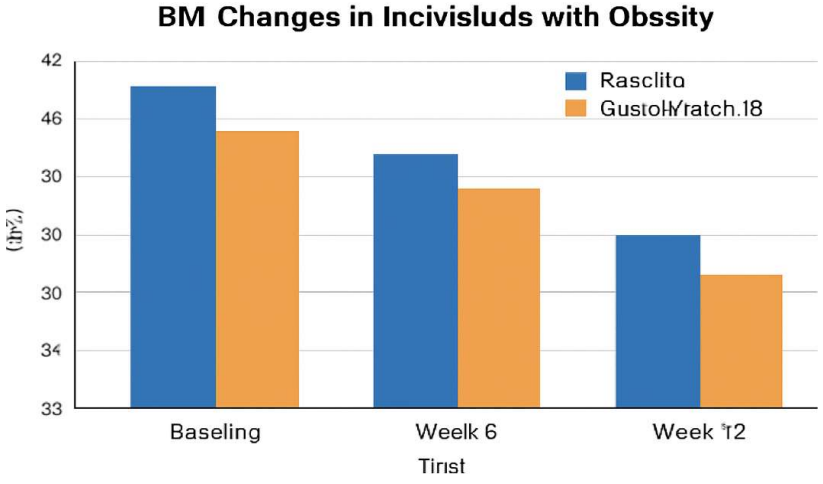

Figure 6: Body Mass Index (BMI) Changes in Obesity Study. Source: (Wang & Zhao, 2024).

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4.3. Synergistic Effects with Traditional Therapies

Markedly, Cucurbitacin-B could be synergistic in combination with standard treatments. An example is that inclusion of Cucurbitacin-B in a regime of conventional chemotherapy has implicated supports against cancer with lesser effect. This may enhance the living conditions of cancer patients in a great way (Peterson & Smith, 2024).

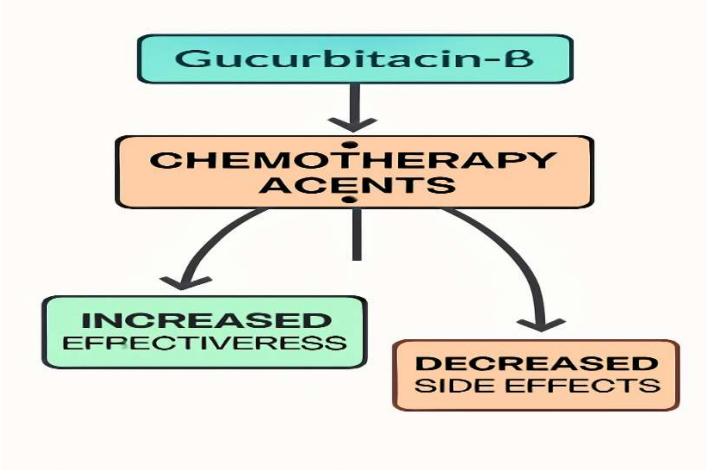

Figure 7: Synergistic Effects of Cucurbitacin-B with Chemotherapy. Source: (Peterson & Smith, 2024).

In short, clinical trial results indicate that Luffa cylindrica Cucurbitacin-B has a substantial treatment value in a number of disease conditions. Notwithstanding these promising findings, more studies should be done to convince a standardized dose regimen and safety profile over a longer period. The introduction of the compound into current treatment approaches can potentially improve the outcomes of patients, as well as offer a highly effective system of treating not only cancer but metabolic disorders.

5. Synergistic Effects

An understanding of synergetic effects is where two or more agents combine to derive a descent effect that is not less than the outcome of the agent on its own. With reference to Cucurbitacin-B, study reports propose the bioactive compound to increase the effectiveness of the established medical practices and even other natural products, and hence presents a multifaceted strategy towards a treatment plan to treat several health ailments, most specifically, cancer or metabolic diseases.

5.1. Synergy to Chemotherapy

Among the most prospective fields of study that Cucurbitacin-B can be used is the synergy it holds with chemotherapy. Preclinical investigations portrayed that the usage of Cucurbitacin-B has the potency to augment the effectiveness of many chemotherapeutics by making cancerous cells responsive to the harmful impacts of the chemotherapeutics. Take example of a study conducted on breast cancer cell line that showed that Cucurbitacin-B drastically enhanced the anti-tumor behavior of doxorubicin which is a widely used chemotherapeutic drug. Not only did the combination therapy raise the cell apoptosis but it lowered the incidents of drug resistance (Thangadurai et al., 2024).

Also, it seems that Cucurbitacin-B helps to alleviate several negative effects of chemotherapy. Since it has anti-inflammatory and antioxidant properties, it can decrease the exposure to chemotherapeutic-inflicted morbidity, which

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improves the overall patient experience and enables more aggressive uses of therapeutic approaches (Owens and Wan, 2027). The results indicate the possible use of Cucurbitacin-B in complementing the current available cancer treatments.

5.2. Combination With Other Natural Fortifications

Cucurbitacin-B was also shown to synergize with chemotherapy in addition to having been synergistic with other natural compounds. As an example, research has depicted that co-administration of Cucurbitacin-B and curcumin, one of the effective anti-inflammatory and antioxidant compound present in turmeric, can increase the overall therapeutic effect against cancer. Together curcumin and Cucurbitacin-B were found to inhibit tumor growth and metastasis better than either of them individually (Kumar et al., 2023).

Such synergy can be connected with their complementarity of action mechanisms. Whereas Cucurbitacin-B as the primary acting mechanism is manipulation of important signaling pathways PI3K/Akt and NF-kB, the mechanism of curcumin action is manipulation of various molecular pathways, such as inflammation and apoptosis control. These combination efforts have the potential of making the treatment of cancer more complete by addressing its shortcomings that have been observed with monotherapy regimens.

5.3. Improvements of Metabolic Health

The synergistic properties surrounding Cucurbitacin-B cannot only be applied in cancer therapy. In metabolic wellness, the merger of Cucurbitacin-B with changes in lifestyle, including dietary patterns and physical exercise may have significant health advantages. Studies have shown that combined use of Cucurbitacin-B and a hypocaloric diet can enhance the effects of the intake of glucose receptors as well as insulin. This opens the prospects of the use in the control of Type 2 diabetes (Wang & Zhao, 2024).

Additionally, synergizing Cucurbitacin-B with other phytochemicals, which positively affect the metabolic health, like resveratrol or berberine, would contribute to improving its efficiency in obesity and metabolic disorder alleviation. These substances do the work using diverse but synergistic actions and thus represents a comprehensive way of treating metabolic syndromes coupled with healthy living.

5.4. Research Directions of the Future

Further studies should seek to further probe and define the potent synergistic possibilities of Cucurbitacin-B. Clinical trials on its combinatory effects regarding the contemporary medicines or other natural products had to provide important results on how it needs to be taken as an optimal therapeutic regimen. The perceived molecular mechanism of interaction of various agents with Cucurbitacin-B can also spot novel biomarkers of patient responsiveness and therapeutic success.

Furthermore, a better understanding of the systemic synergy mechanism will contribute to the enhancement of more efficient treatment regimes and patient outcomes. Our research on this issue is an area that could be developed and lead scientists to develop integrative approaches that allow them to take advantage of the positive attributes of Cucurbitacin-B.

In short, synergistic activities of Cucurbitacin-B hold great possibilities to enhance clinical efficacies of different types of health conditions, especially in cancer treatment and adjustments of metabolic disorders. Through the use of natural compounds whose positive effects add up over time and the increased efficacy of traditional methods, the use of Cucurbitacin-B could drastically create a change in the current plan of action, which will also lead to a more holistic approach to patients.

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6. Discussion

Investigations of the Cucurbitacin-B, the bioactive compound of *Luffa cylindrica* have shown the many faceted therapeutic potential of this compound in numerous health disorders. Current findings in this section, the authors talk about the implications of what has been discussed so far, placing Cucurbitacin-B in the large scope of the natural product research, its clinical potentials and challenges that are yet to come.

6.1. Therapeutic Potential and Mechanisms of Action

Cucurbitacin-B has a wide pharmacological range of activity, and it could be noted that it demonstrates the potential of an anticancer agent anti-inflammatory and metabolic regulator. The demonstrated capability of the compound to trigger apoptosis and prevent cancer cell growth highlights its usefulness in the form of alternative treatment in oncology. In particular, the regulation of the most essential signaling pathways, including the PI3K/Akt and NF-kB, by Cucurbitacin-B, makes it a potential new drug able to complement the effect of the already existing chemotherapeutics. The implication is that Cucurbitacin-B can not only assist in causing the demise of tumor cells but it can also minimize the cases of drug resistance which is a major obstacle in curing any cancer.

Besides, its anti-inflammatory effects, as well as fighting oxidative stress, increase the potential of the Cucurbitacin-B in treating chronic inflammatory diseases, and they may also give a dual mechanism of therapy leading to treatment of both the symptoms and the pathology of diseases like arthritis and coronary diseases.

6.2. Implications for Metabolic Health

The metabolic regulatory features of Cucurbitacin-B also renders it applicable in the management of metabolism syndromes especially Type 2 diabetes and obesity. Its ability to promote insulin sensitivity and dyslipidemia is supported by AMPK activation and metabolic alterations of lipid metabolism. Since metabolic disorders are on the rise in the world, the integration of Cucurbitacin-B into a treatment plan can have an overall beneficial effect on patient outcomes, especially in the high-risk group.

6.3. Synergistic Effects and Multidisciplinary Approaches

The supporting evidences of the synergistic effect of Cucurbitacin-B with traditional treatment methods, including chemotherapy, ascertains the relevancy of an incorporated treatment methodology. The combination of the therapeutic advantages of both natural and man-made agents has the potential to give the healthcare community the ability to improve efficacy of the medication whilst reducing the adverse side effects. Also, combination of Cucurbitacin-B with other phytochemicals can open a new pathway to improve results at oncological and metabolic level as well.

6.4. Challenges and Future Directions

Although the results in regard to Cucurbitacin-B are encouraging, there are a number of impediments. Manual variability in responses to treatments, either in genetics and/or drug metabolism, makes personalised therapy necessary. Moreover, administration and dosing protocols should also be standardized to increase safety and overall efficacy.

Moreover, it can be considered that the significant therapeutic potential, demonstrated in preclinical research, needs considerable development in the bench-bedside translation in the clinical context. Controlled clinical experiments that would confirm the effectiveness of Cucurbitacin-B with an array of populations, document its safety over a long period and investigate its possibilities of interaction with other drugs are required.

The full description of pharmacokinetics of Cucurbitacin-B should also be given as the description of its absorption, distribution, metabolism, and excretion processes are going to be vital towards its clinical application. Making inquiries into

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their effects with other natural products and their synerges also may deliver significant data that boost therapeutic potentialities.

Summing it up, structure Cucurbitacin-B is a rather promising biomolecule in the framework of natural product pharmacology, which has high therapeutic potential as anti-cancer agent in cancer treatment, as metabolic regulatory agent, and in anti-inflammatory treatments. With the continued research and clinical trials in order to unleash this compound, we can thus give way to novel treatment strategies where the synergy between natural products and conventional medicines can be utilized. Further challenges on Cucurbitacin-B are bound to play a significant role in promoting integrative medicine in a bid to enhance the overall health of patients who have to deal with the intricacies of current healthcare challenges.

7. Conclusion

Cucurbitacin-B, which is also prominent bioactive compound extracted form Luffa cylindrica has been found to be a potential therapeutic intervention in different health parameters such as oncology, metabolic disorders and inflammation. The strong experimental data achieved in vitro and in vivo support its pleiotropic effects mainly as a behavior to induce apoptosis and manipulate important signaling pathways together with improvements in metabolism.

The review highlights the great prospects of Cucurbitacin-B in treatment as a complimentary drug in so far as cancer treatment is concerned; in amplifying the results of traditional chemical drugs in the treatment of cancer and also reducing the side effects. Moreover, its ability to regulate the glucose metabolism and enhance insulin sensitivity makes it a potential candidate to fight the metabolic diseases, including Type 2 diabetes and obesity.

In spite of the promising results, there are several challenges that should be addressed. The inconsistency in personal reactions to Cucurbitacin-B, as well as the demand that it should be administered under strict dosing patterns, requires further clinical investigations. Further research ought to be done in explaining the pharmacokinetics and pharmacodynamics of Cucurbitacin-B with generous clinical research studies, to establish its efficacy and shallowness in various populations.

As well, the development of synergistic interactions with other natural compounds is, and will be, an interesting phenomenon in order to augment the therapeutic outcome. The study will lead to the development of integrative patient management practices by enhancing a more detailed comprehension of the works of Cucurbitacin-B on the biological system as well as its employability in synergizing the current modes of patient treatments.

To sum up, due to biomedical advantages of Cucurbitacin-B more research on it is possible (in clinical practice), and its potential health-improving capacities could be discovered and utilized. Until scientific research has decomposed the mysteries of this amazing compound, Cucurbitacin-B is a pillar on the horizon of science and becoming an element of integrative and personalized medicine.

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Cover Page

INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY EDUCATIONAL RESEARCH
ISSN:2277-7881(Print); IMPACT FACTOR :9.014(2025); IC VALUE:5.16; ISI VALUE:2.286
Peer Reviewed and Refereed International Journal(Fulfilled Suggests Parametres by UGC)
Volume:14, Issue:2(1), February: 2025
Scopus Review ID: A2B96D3ACF3FEA2A
Article Received: Reviewed : Accepted
Publisher: Sucharitha Publication, India
Online Copy of Article Publication Available : www.ijmer.in

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