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Anticancer Activity of *Allium cepa* through the Inactivation of NF-κB Pathway: A Literature-based Study

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Abstract: *Allium cepa* (onion) is a bulbous herb renowned for its diverse health benefits. This study aims to summarize the anticancer potential of *A. cepa* through the inactivation of the Nuclear Factor kappa-light-chain-enhancer of activated B cells (NF-κB) pathway by reviewing experimental findings across various cancer models. A thorough examination of the literature was carried out using databases like Google Scholar, PubMed, Web of Science, and ScienceDirect. The findings revealed that phytochemicals such as stigmasterol, fisetin, quercetin, isorhamnetin, morin, kaempferol, luteolin, β-carotene, and β-sitosterol exhibit strong anticancer properties against various cancers, including breast, bladder, colon, colorectal, cervical, lung, liver, oral, pancreatic, and skin cancer, as supported by both *in vivo* and *in vitro* studies. These phytochemicals primarily exert their anticancer effects by blocking the NF-κB signaling pathway. However, further clinical research is needed to investigate its *in vivo* and *in vitro* study to determine its safety and efficacy in cancer treatment, with a focus on optimizing its therapeutic nature.

Keywords: *Allium cepa*; Cancer; NF-κB inhibitor; Phytochemicals; Quercetin

1. Introduction

Natural products are the chemical substances that are synthesized by living organisms (Hasan et al., 2025; Al Hasan et al., 2025; Yana et al., 2025). Since the earliest time, natural resources have been used as a prime provenance for shelter, food, and therapeutic agents, and remarkable research also has been done on phytochemicals for the development of new therapeutic substances with lower side effects (Sharma et al., 2025; Aktar et al., 2024; Bithi et al., 2025). From some evidence, it has been reported that several natural products, for instance, polyphenols, alkaloids, flavonoids, etc., are used to treat cancer via affecting the expression of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB). However, NF-κB has numerous functions, including injury, inflammation, and malignancy. In the term of cancer, its activation has been connected to cell survival, proliferation, angiogenesis, and invasion. In contrast, natural substances inhibit translocation and decrease the LPS-mediated action of NF-κB and suppress the degradation of NF-κB inhibitor alpha (IκBα), NF-κB kinase alpha (IKKα), and IKK-β (Brown et al., 2008; Chauhan et al., 2022).

A. cepa is one of the flavonoid materials found in onion and is the prime representative genus of the Liliaceae family, which consists of over 20 times more quercetin (Kang et al., 2015). It also contains other phytochemical compounds such as flavonol quercetin, phenolic, etc., and is rich in carbohydrates, proteins, potassium, sodium, and phosphorus (Kumar et al., 2013). It has various pharmacological effects such as anti-inflammation (Ullah et al., 2022), anti-hypertensive (Tong et al., 2021), anti-oxidant (Alpsoy et al., 2013), anti-thrombotic (Yamada et al., 2004), anti-cancer (Al Hasan et al., 2024; Fadholly et al., 2019), anti-diabetic (Jini & Sharmila, 2020), etc.

The aim of this study is to summarize the anticancer mechanism of *A. cepa* through the inactivation of the NF-κB pathway by collecting information from previous literature.

2. Methodology

2.1. Literature search strategy

A literature review was conducted in well-established scientific databases: PubMed, Google Scholar, Science Direct, Web of Science,

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etc., using some keywords: *Allium cepa*, anti-cancer, NF-κB, phytochemicals, activity, etc. No language limitations were imposed.

2.2. Inclusion criteria

The following inclusion criteria were used:
1. Studies with anticancer actions from several sources.
2. Studies carried out *in vitro, in vivo*, or *ex vivo* with or without animals used in experiments.
3. Studies that include or exclude the mechanism of action.

2.3. Exclusion criteria

The following exclusion criteria were used:
1. Titles and/or abstracts that do not match the requirements of inclusion and duplication of data.
2. Anti-cancer activity, with other research not clarifying the present study topic.

3. Results and discussion

3.1. Primary phytochemicals

A. cepa and other plant sources include phytochemicals that have strong anticancer properties, mostly by blocking the NF-κB signaling pathway (Marefati et al., 2021). For example, in colon cancer cell lines (Caco-2, HCT116, and HT29), quercetin and fisetin from onions have shown strong anti-proliferative effects at doses ranging from 12.5 to 240 μM, with IC_{50} values as low as 20 μM. Similarly, NF-κB inhibition in colorectal, cervical, and oral cancers has been demonstrated by crude extracts of onion peel and other phytochemicals such as isorhamnetin, stigmasterol, and kaempferol etc. Tested in both *in vitro* and *in vivo* models, these compounds demonstrate the therapeutic potential of phytochemicals derived from *A. cepa* in targeting NF-κB, a crucial regulator of inflammation and the progression of cancer.

3.2. Anticancer mechanism through NF-κB

The NF-κB signaling pathway plays a crucial role in the cancer stage's progression, such as metastasis, proliferation, and apoptosis (Ayaz et al., 2022). Furthermore, this pathway has been associated with tumor initiation, progression, and chemotherapy resistance (Perkins, 2012; Nakanishi & Toi, 2005). According to a vast amount of evidence, NF-κB signaling inhibition could be efficient in suppressing tumor development (Fuchs, 2010; Kim et al., 2006). *A. cepa* has a vital part in the treatment of cancer via different mechanisms, including NF-κB pathways, and various studies recommend that the risk of cancer reduces due to *A. cepa* (Pareek et al., 2017). In our study, stigmasterol from vegetables and fruits demonstrated efficacy against breast cancer in MDA-MB-231 and MCF-7 cell lines at concentrations ranging from 35–560 μM (Omran et al., 2024). Similarly, fisetin from smoke trees and onions showed potential against bladder cancer (T24, EJ, and J82 cell lines) and colon cancer (HCT116 and HT29 cell lines) at concentrations of 60–100 μM and 30–240 μM, respectively, with IC_{50} values of 107.6 μM and 43.4 μM for colon cancer (Li et al., 2011; Suh et al., 2009). Quercetin, found in onions, exhibited activity against colon cancer (Caco-2, SW 620 cell lines) and oral cancer (SAS cell line) at concentrations of 12.5-200 μM and 25-400 μM, respectively, with IC_{50} values of 35 μM and 20 μM for colon cancer (Han et al., 2016; Zhang et al., 2015; Lai et al., 2013). Isorhamnetin, a metabolite, and morin from *Ficus carica* were effective against colon cancer in HCT-116 cell lines and male albino *Wistar* rats at 20–100 μM and 50 mg/kg, respectively (Jaramillo et al., 2010; Sharma et al., 2018). Kaempferol, a natural flavonoid, showed promise against cervical cancer (HeLa cell line) with an IC_{50} of 50 μM (Afroze et al., 2022). Luteolin from *Lonicera japonica Thunb.* and *Chrysanthemum indicum* L. was effective against lung cancer (NCI-H292 cell lines) (Lee et al., 2015), while β-carotene from *Gracillaria sp.* demonstrated activity against liver cancer (HepG2 cell line) with an IC_{50} of 10.5 μM (Kavalappa et al., 2019). Ferulic acid from fruits and vegetables was effective against oral cancer in male golden *Syrian* hamsters at 40 mg/kg (Manoharan et al., 2014). Fisetin and β-sitosterol showed potential against pancreatic cancer in AsPC-1 and MIA-PaCa-2 cell lines at concentrations of 10–80 μM and 100–500 μM/L, respectively, with IC_{50} values of 38 μM and 248.6 μM (Murtaza et al., 2009; Cao et al., 2019). Isorhamnetin from *Persicaria thunbergii* H. and *Elaeagnus rhamnoides* (L.) was effective against skin cancer (B16F10 cell line) at 10–100 μmol/L (Duan et al., 2020).

Moreover, NF-κB is activated and contributes to increased proliferation in colon cancer cells (Sasaki et al., 2001; Wu et al., 2008; Kang et al., 2008). Besides, NF-κB is an essential inhibitor of apoptosis and can give protection to cancer cells induced via TNFα from cell death (Luo et al., 2005). The findings of our study highlight the potential of *A. cepa* as anticancer agents through NF-κB inhibition across various cancer types. The phytochemicals, tested in both *in vitro* cell lines and *in vivo* animal models, consistently inhibited NF-κB, a key pathway regulating tumor growth, metastasis, and inflammation, demonstrating their potential as effective anticancer agents. Further studies should focus on isolating bioactive compounds in *A. cepa* responsible for NF-κB inhibition to enhance targeted cancer treatment. Additionally, clinical trials are needed to validate its efficacy and safety in human cancer treatment. The anticancer activity of *A. cepa* across various cancers, as reported in the literature, is summarized in **Table 1**, while its possible mechanism of action is illustrated in **Fig. 1**.

A clinical trial is a research study that tests the safety and effectiveness of a new drug in humans, playing a critical role in drug discovery by ensuring treatments are safe and beneficial before approval (Downing et al., 2014). Clinical trials investigating

Table 1. Mechanism of NF-κB in anticancer activity of *Allium cepa.*

Sources	Phytochemicals	Cancer types	Experimental model/ cell lines	Tested concentrations, (R/A)	IC_{50}	Mechanisms	References
Vegetables and fruits	Stigmasterol	Breast cancer	MDA-MB-231 and MCF-7 cell line, *in vitro*	35–560 μM	-	↓NF-κB	Omran et al., 2024
Smoke tree	Fisetin	Bladder cancer	T24, EJ and J82 cell lines, *in vitro*	60–100 μM for 48 h	-	↓NF-κB	Li et al., 2011
Onions	Quercetin	Colon cancer	Caco-2 cell lines, *in vitro*	20-100 μM for 24 h	-	↓NF-κB	Han et al., 2016
Red onions	Quercetin	Colon cancer	Caco-2, SW-620 cell lines, *in vitro*	12.5–200 μM for 24 h	35 μM, 20 μM	↓NF-κB	Zhang et al., 2015
Onion	Fisetin	Colon cancer	HCT116, HT29 cell lines, *in vitro*	30–240 μM for 24, 48, 72 and 96 h.	107.6 μM, 43.4 μM	↓NF-κB	Suh et al., 2009

Table 1. *Continued*

Sources	Phytochemicals	Cancer types	Experimental model/ cell lines	Tested concentrations, (R/A)	IC_{50}	Mechanisms	References
An immediate 3'-O-methylated metabolite	Isorhamnetin	Colon Cancer	HCT-116 cell line, *in vitro*	20–100 μM for 24-48 h	72 μM	↓NF-κB	Jaramillo et al., 2010
Ficus carica	Morin	colon cancer	Male albino Wistar rats, *in vivo* (n=6)	50 mg/kg (i.p.)	-	↓NF-κB	Sharma et al., 2018
Crude extracts of onion peel	-	Colorectal cancer	HT-29, HUVECs cell lines, *in vitro*	1–100 μg/mL	-	↓NF-κB	Pareek et al., 2017
A natural flavonoid	Kaempferol	Cervical cancer	HeLa cell line, *in vitro*	1–100 μM for 24 h and 48 h	50 μM	↓NF-κB	Afroze et al., 2022
Lonicera japonica Thunb. *Chrysanthemum indicum* L.	Luteolin	Lung cancer	NCI-H292 cell lines, *in vitro*	-	-	↓NF-κB	Lee et al., 2015
Gracillaria sp.	β-carotene	Liver cancer	HepG2 cell line, *in vitro*	1 and 5 μM for 8h	10.5 μM	↓NF-κB	Kavalappa et al., 2019
Onions	Quercetin	Oral cancer	SAS cell line, *in vitro*	25–400 μM for 24 h	-	↓NF-κB	Lai et al., 2013
Fruits and Vegetables	Ferulic acid	Oral cancer	Male golden Syrian hamsters, *in vivo* (n=10)	40 mg/kg (p.o.)	-	↓NF-κB	Manoharan et al., 2014
A natural flavonoid	Fisetin	Pancreatic cancer	AsPC-1 cell lines, *in vitro*	10–80 μM for 24 and 48 h	38 μM	↓NF-κB	Murtaza et al., 2009
Bioactive constituent present in plants	β-sitosterol	Pancreatic cancer	MIA-PaCa-2 cell line, *in vitro*	100–500 μM/L for 24–72h	248.6 μM	↓NF-κB	Cao et al., 2019
Persicaria thunbergii H. *Elaeagnus rhamnoides* (L.)	Isorhamnetin	Skin cancer	B16F10 cell line, *in vitro*	10–100 μmol/L for 24 h	-	↓NF-κB	Duan et al., 2020

↑: Increase; ↓: decrease; NF-κB: Nuclear Factor kappa-light-chain-enhancer of activated B cells;

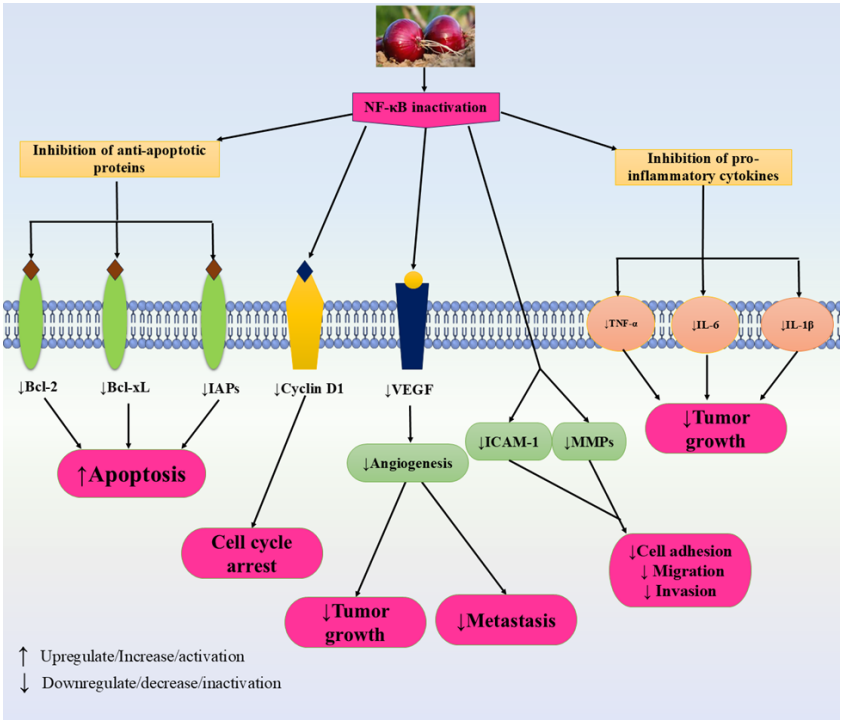

Fig. 1. Possible mechanism of NF-κB in anticancer activity of *A. cepa.* [This figure illustrates the anticancer mechanisms of *A. cepa* through the inactivation of Nuclear Factor-kappa B (NF-κB). Suppression of NF-κB leads to the downregulation of anti-apoptotic proteins, including B-cell lymphoma 2 (Bcl-2), B-cell lymphoma-extra-large (Bcl-xL), and Inhibitor of Apoptosis Proteins (IAPs), thereby promoting apoptosis. NF-κB inactivation also decreases Cyclin D1, a protein crucial for cell cycle progression, leading to increased cell cycle arrest. Additionally, it reduces the levels of pro-inflammatory cytokines such as Tumor Necrosis Factor-alpha (TNF-α), Interleukin-6 (IL-6), and Interleukin-1 beta (IL-1β), thereby limiting tumor growth. Furthermore, NF-κB inhibition leads to a decrease in Intercellular Adhesion Molecule-1 (ICAM-1) and Matrix Metalloproteinases (MMPs), which in turn inhibits cell adhesion, migration, and invasion. By reducing Vascular Endothelial Growth Factor (VEGF) levels, this natural compound effectively suppresses tumor growth and metastasis.]

phytochemicals such as stigmasterol, fisetin, quercetin, isorhamnetin, morin, kaempferol, luteolin, β-carotene, and β-sitosterol have shown promising potential in cancer treatment. These naturally occurring compounds, found in various plant-based foods, have been studied for their ability to modulate key pathways involved in cancer progression. For instance, fisetin (100 mg daily) has demonstrated efficacy in lowering inflammatory markers in colorectal cancer patients (Farsad-Naeimi et al., 2018). Furthermore, clinical evidence indicates quercetin (500 mg daily for 8 weeks) may reduce inflammation and oxidative stress in cancer patients (Askari et al., 2012). Although preclinical studies highlight their benefits, well-designed clinical trials are essential to assess safety profiles and validate the efficacy of these phytochemicals in diverse cancer types.

4. Conclusion

To recapitulate, there are various health benefits associated with *A. cepa*. It lessens the cancer risks based on the numerous experimental works. Compounds such as quercetin, fisetin, isorhamnetin, kaempferol, ferulic acid, luteolin, morin, stigmasterol, β-sitosterol, and β-carotene have demonstrated efficacy in inhibiting NF-κB across a range of cancer types, including colorectal, oral, colon, bladder, pancreatic, skin, cervical, lung, and breast cancers. These phytochemicals were tested in both *in vitro* cell lines and *in vivo* animal models, showing consistent inhibition of NF-κB, which is crucial for reducing tumor growth, metastasis, and inflammation. The findings suggest that targeting the NF-κB pathway with these natural compounds could be a promising therapeutic strategy for cancer treatment. However, more evidence and documentation of *A. cepa* are required in terms of clinical trials to validate the claims of anti-cancer activity.

Conflict of interest

The authors declared no conflict.

Ethical statement

This study was not conducted with any human or animal subjects.

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Not applicable.

Data availability

Data will be made available on request.

Authorship contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation or in all these areas that is, revising or critically reviewing the article; giving final approval of the version to be published; agreeing on the journal to which the article has been submitted; and confirming to be accountable for all aspects of the work. All authors have read and agreed to the published version of the manuscript.

References

Afroze, N., Pramodh, S., Almutary, A. G., Rizvi, T. A., Rais, N., Raina, R., ... & Hussain, A. (2022). Kaempferol regresses carcinogenesis through a molecular cross talk involved in proliferation, apoptosis and inflammation on human cervical cancer cells, HeLa. *Applied Sciences*, *12*(6), 3155. https://doi.org/10.3390/app12063155

Aktar, A., Bhuia, S., Chowdhury, R., Ferdous, J., Khatun, M., Hasan, S. A., Mia, E., Hasan, R., & Islam, M. T. (2024). An Insight of Plant Source, Toxicological Profile, and Pharmacological Activities of Iridoid Loganic Acid: A ComprehensiveReview. *Chemistry & biodiversity*, 21 (12), e202400874. https://doi.org/10.1002/cbdv.202400874

Al Hasan, M. S., Bhuia, M. S., Chowdhury, R., Shadin, M., Mia, E., Yana, N. T., ... & Islam, M. T. (2025). Anticancer activity of Jasminum sambac and its bioactive phytochemicals against the PI3K-AKT-mTOR pathway: A literature-based in silico study. *South African Journal of Botany*, 180, 431-443. https://doi.org/10.1016/j.sajb.2025.03.004

Al Hasan, M. S., Mia, E., Yana, N. T., Rakib, I. H., Bhuia, M. S., Chowdhury, R., ... & Islam, M. T. (2024). Allium cepa bioactive phytochemicals as potent ALK (Anaplastic lymphoma kinase) inhibitors and therapeutic agents against non-small cell lung cancer (NSCLC): A computational study. *Pharmacological Research-Natural Products*, *5*, 100124. https://doi.org/10.1016/j.prenap.2024.100124

Alpsoy, S., Aktas, C., Uygur, R., Topcu, B., Kanter, M., Erboga, M., Karakaya, O., & Gedikbasi, A. (2013). Antioxidant and anti-apoptotic effects of onion (Allium cepa) extract on doxorubicin-induced cardiotoxicity in rats. *Journal of applied toxicology: JAT*, *33*(3), 202–208. https://doi.org/10.1002/jat.1738

Askari, G., Ghiasvand, R., Feizi, A., Ghanadian, S. M., & Karimian, J. (2012). The effect of quercetin supplementation on selected markers of inflammation and oxidative stress. *Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences*, *17*(7), 637.

Ayaz, M., Nawaz, A., Ahmad, S., Mosa, O. F., Eisa Hamdoon, A. A., Khalifa, M. A., ... & Ananda Murthy, H. C. (2022). Underlying anticancer mechanisms and synergistic combinations of phytochemicals with cancer chemotherapeutics: potential benefits and risks. *Journal of Food Quality*, *2022*(1), 1189034. https://doi.org/10.1155/2022/1189034

Bithi, S. A., Al Hasan, M. S., Bhuia, M. S., Mia, E., Yana, N. T., Hasan, A. M. W., Uddin, M. B., Sayeed, M. A., Emon, Y., Hasan, R., Chowdhury, R., & Islam, M. T. (2025). Botanical sources, biopharmaceutical profile, anticancer effects with mechanistic insight, toxicological and clinical evidence of prunetin: a literature review. *Medical oncology* (Northwood, London, England), 42(4), 87. https://doi.org/10.1007/s12032-025-02646-z

Brown, M., Cohen, J., Arun, P., Chen, Z., & Van Waes, C. (2008). NF-kappaB in carcinoma therapy and prevention. *Expert opinion on therapeutic targets*, *12*(9), 1109–1122. https://doi.org/10.1517/14728222.12.9.1109

Cao, Z. Q., Wang, X. X., Lu, L., Xu, J. W., Li, X. B., Zhang, G. R., Ma, Z. J., Shi, A. C., Wang, Y., & Song, Y. J. (2019). β-Sitosterol and Gemcitabine Exhibit Synergistic Anti-pancreatic Cancer Activity by Modulating Apoptosis and Inhibiting Epithelial-Mesenchymal Transition by Deactivating Akt/GSK-3β Signaling. *Frontiers in pharmacology*, *9*, 1525. https://doi.org/10.3389/fphar.2018.01525

Chauhan, A., Islam, A. U., Prakash, H., & Singh, S. (2022). Phytochemicals targeting NF-κB signaling: Potential anti-cancer interventions. *Journal of pharmaceutical analysis*, *12*(3), 394–405. https://doi.org/10.1016/j.jpha.2021.07.002

Downing, N. S., Aminawung, J. A., Shah, N. D., Krumholz, H. M., & Ross, J. S. (2014). Clinical trial evidence supporting FDA approval of novel therapeutic agents, 2005-2012. *JAMA*, *311*(4), 368–377. https://doi.org/10.1001/jama.2013.282034

Duan, R., Liang, X., Chai, B., Zhou, Y., Du, H., Suo, Y., Chen, Z., Li, Q., & Huang, X. (2020). Isorhamnetin Induces Melanoma Cell Apoptosis via the PI3K/Akt and NF-κB Pathways. *BioMed research international*, *2020*, 1057943. https://doi.org/10.1155/2020/1057943

Fadholly, A., Ansori, A. N., Jayanti, S., Proboningrat, A., Kusala, M. K., Putri, N., ... & Sudjarwo, S. A. (2019). Cytotoxic effect of Allium cepa L. extract on human colon cancer (WiDr) cells: in vitro study. *Research Journal of Pharmacy and Technology*, *12*(7), 3483-3486.

Farsad-Naeimi, A. Alizadeh, M., Esfahani, A., & Darvish Aminabad, E., (2018). Effect of fisetin supplementation on inflammatory factors and matrix metalloproteinase enzymes in colorectal cancer patients. *Food & function*, *9*(4), 2025–2031. https://doi.org/10.1039/c7fo01898c

Fuchs O. (2010). Transcription factor NF-κB inhibitors as single therapeutic agents or in combination with classical chemotherapeutic agents for the treatment of hematologic malignancies. *Current molecular pharmacology*, *3*(3), 98–122. https://doi.org/10.2174/1874467211003030098

Han, M., Song, Y., & Zhang, X. (2016). Quercetin Suppresses the Migration and Invasion in Human Colon Cancer Caco-2 Cells Through Regulating Toll-like Receptor 4/Nuclear Factor-kappa B Pathway. *Pharmacognosy magazine*, *12*(Suppl 2), S237–S244. https://doi.org/10.4103/0973-1296.182154

Hasan, A. M. W., Al Hasan, M. S., Mizan, M., Miah, M. S., Uddin, M. B., Mia, E., ... & Islam, M. T. (2025). Quercetin promises anticancer activity through PI3K-AKT-mTOR Pathway: a literature review. *Pharmacological Research-Natural Products*, 100206. https://doi.org/10.1016/j.prenap.2025.100206

Jaramillo, S., Lopez, S., Varela, L. M., Rodriguez-Arcos, R., Jimenez, A., Abia, R., Guillen, R., & Muriana, F. J. (2010). The flavonol isorhamnetin exhibits cytotoxic effects on human colon cancer cells. *Journal of agricultural and food chemistry*, *58*(20), 10869–10875. https://doi.org/10.1021/jf102669p

Jini, D., & Sharmila, S. J. M. T. P. (2020). Green synthesis of silver nanoparticles from Allium cepa and it's in vitro antidiabetic activity. *Materials Today: Proceedings*, *22*, 432-438. https://doi.org/10.1016/j.matpr.2019.07.672

Kang, B. K., Kim, K. B. W. R., Ahn, N. K., Choi, Y. U., Kim, M. J., Bark, S. W., ... & Ahn, D. H. (2015). Anti-inflammatory effect of onion (Allium cepa) peel hot water extract in vitro and in vivo. *KSBB Journal*, *30*(4), 148-154. https://doi.org/10.7841/ksbbj.2015.30.4.148

Kang, M. J., Ryu, B. K., Lee, M. G., Han, J., Lee, J. H., Ha, T. K., Byun, D. S., Chae, K. S., Lee, B. H., Chun, H. S., Lee, K. Y., Kim, H. J., & Chi, S. G. (2008). NF-kappaB activates transcription of the RNA-binding factor HuR, via PI3K-AKT signaling, to promote gastric tumorigenesis. *Gastroenterology*, *135*(6), 2030–2042.e20423. https://doi.org/10.1053/j.gastro.2008.08.009

Kavalappa, Y.P., et al., β-carotene isolated from the marine red alga, Gracillaria sp. potently attenuates the growth of human hepatocellular carcinoma (HepG2) cells by modulating multiple molecular pathways. 2019. 52: p. 165-176. https://doi.org/10.1016/j.jff.2018.11.015

Kim, H. J., Hawke, N., & Baldwin, A. S. (2006). NF-kappaB and IKK as therapeutic targets in cancer. *Cell death and differentiation*, *13*(5), 738–747. https://doi.org/10.1038/sj.cdd.4401877

Kumar, K. E., Harsha, K. N., & Sudheer, V. (2013). In vitro antioxidant activity and in vivo hepatoprotective activity of aqueous extract of Allium cepa bulb in ethanol induced liver damage in Wistar rats. *Food Science and Human Wellness*, *2*(3-4), 132-138. https://doi.org/10.1016/j.fshw.2013.10.001

Lai, W. W., Hsu, S. C., Chueh, F. S., Chen, Y. Y., Yang, J. S., Lin, J. P., Lien, J. C., Tsai, C. H., & Chung, J. G. (2013). Quercetin inhibits migration and invasion of SAS human oral cancer cells through inhibition of NF-κB and matrix metalloproteinase-2/-9 signaling pathways. *Anticancer research*, *33*(5), 1941–1950.

Lee, H. J., Seo, H. S., Ryu, J., Yoon, Y. P., Park, S. H., & Lee, C. J. (2015). Luteolin inhibited the gene expression, production and secretion of MUC5AC mucin via regulation of nuclear factor kappa B signaling pathway in human airway epithelial cells. Pulmonary pharmacology & therapeutics, 31, 117–122. https://doi.org/10.1016/j.pupt.2014.09.008

Li, J., Cheng, Y., Qu, W., Sun, Y., Wang, Z., Wang, H., & Tian, B. (2011). Fisetin, a dietary flavonoid, induces cell cycle arrest and apoptosis through activation of p53 and inhibition of NF-kappa B pathways in bladder cancer cells. *Basic & clinical pharmacology & toxicology*, *108*(2), 84–93. https://doi.org/10.1111/j.1742-7843.2010.00613.x

Luo, J. L., Kamata, H., & Karin, M. (2005). IKK/NF-kappaB signaling: balancing life and death--a new approach to cancer therapy. *The Journal of clinical investigation*, *115*(10), 2625–2632. https://doi.org/10.1172/JCI26322

Manoharan, S., Rejitharaji, T., M Prabhakar, M., Manimaran, A., & B Singh, R. (2014). Modulating Effect of Ferulic Acid on NF-kB, COX-2 and VEGF Expression Pattern During 7, 12-Dimethylbenz (a) anthracene Induced Oral Carcinogenesis. *The Open Nutraceuticals Journal*, *7*(1).

Marefati, N., Ghorani, V., Shakeri, F., Boskabady, M., Kianian, F., Rezaee, R., & Boskabady, M. H. (2021). A review of anti-inflammatory, antioxidant, and immunomodulatory effects of *Allium cepa* and its main constituents. *Pharmaceutical biology*, *59*(1), 287–302. https://doi.org/10.1080/13880209.2021.1874028

Murtaza, I., Adhami, V. M., Hafeez, B. B., Saleem, M., & Mukhtar, H. (2009). Fisetin, a natural flavonoid, targets chemoresistant human pancreatic cancer AsPC-1 cells through DR3-mediated inhibition of NF-kappaB. *International journal of cancer*, *125*(10), 2465–2473. https://doi.org/10.1002/ijc.24628

Nakanishi, C., & Toi, M. (2005). Nuclear factor-kappaB inhibitors as sensitizers to anticancer drugs. *Nature reviews. Cancer*, *5*(4), 297–309. https://doi.org/10.1038/nrc1588

Omran, G., Abd-Alhaseeb, M., & HOUSSEN, M. (2024). Chemotherapeutic effect of stigmasterol in sorafenib treated breast cancer cell lines via modulation of NF-κB and ERK signaling pathways. *Egyptian Journal of Chemistry*, *67*(3), 227-234. https://doi.org/10.21608/ejchem.2023.204388.7825

Pareek, S., Sagar, N. A., Sharma, S., & Kumar, V. (2017). Onion (allium cepa L.). *Fruit and Vegetable Phytochemicals: Chemistry and Human Health, 2nd Edition*, 1145-1162.

Perkins N. D. (2012). The diverse and complex roles of NF-κB subunits in cancer. *Nature reviews. Cancer*, *12*(2), 121–132. https://doi.org/10.1038/nrc3204

Sasaki, N., Morisaki, T., Hashizume, K., Yao, T., Tsuneyoshi, M., Noshiro, H., Nakamura, K., Yamanaka, T., Uchiyama, A., Tanaka, M., & Katano, M. (2001). Nuclear factor-kappaB p65 (RelA) transcription factor is constitutively activated in human gastric carcinoma tissue. *Clinical cancer research: an official journal of the American Association for Cancer Research*, *7*(12), 4136–4142.

Sharma, K. K., Al Hasan, M. S., Rouf, R., Emon, Y., Mia, E., Hossan, R., ... & Islam, M. T. (2025). Assessment of antiemetic and modulatory activity of dihydrocoumarin on copper sulfate induced emetic chicks: An in vivo investigation. *Food Chemistry Advances*, *6*, 100930. https://doi.org/10.1016/j.focha.2025.100930

Sharma, S. H., Kumar, J. S., Chellappan, D. R., & Nagarajan, S. (2018). Molecular chemoprevention by morin - A plant flavonoid that targets nuclear factor kappa B in experimental colon cancer. *Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie*, *100*, 367–373. https://doi.org/10.1016/j.biopha.2018.02.035

Suh, Y., Afaq, F., Johnson, J. J., & Mukhtar, H. (2009). A plant flavonoid fisetin induces apoptosis in colon cancer cells by inhibition of COX2 and Wnt/EGFR/NF-kappaB-signaling pathways. *Carcinogenesis*, *30*(2), 300–307. https://doi.org/10.1093/carcin/bgn269

Tong, T., Wang, Y. N., Zhang, C. M., & Kang, S. G. (2021). *In vitro* and *in vivo* antihypertensive and antioxidant activities of fermented roots of *Allium hookeri*. *Chinese herbal medicines*, *13*(4), 541–548. https://doi.org/10.1016/j.chmed.2021.08.003

Ullah, H., Minno, A. D., Santarcangelo, C., Tantipongpiradet, A., Dacrema, M., Matteo, R. D., El-Seedi, H. R., Khalifa, S. A. M., Baldi, A., Rossi, A., & Daglia, M. (2022). *In Vitro* Bioaccessibility and Anti-Inflammatory Activity of a Chemically Characterized *Allium cepa* L. Extract Rich in Quercetin Derivatives Optimized by the Design of Experiments. *Molecules (Basel, Switzerland)*, *27*(24), 9065. https://doi.org/10.3390/molecules27249065

Wu, L., Pu, Z., Feng, J., Li, G., Zheng, Z., & Shen, W. (2008). The ubiquitin-proteasome pathway and enhanced activity of NF-kappaB in gastric carcinoma. *Journal of surgical oncology*, *97*(5), 439–444. https://doi.org/10.1002/jso.20952

Yamada, K., Naemura, A., Sawashita, N., Noguchi, Y., & Yamamoto, J. (2004). An onion variety has natural antithrombotic effect as assessed by thrombosis/thrombolysis models in rodents. *Thrombosis research*, *114*(3), 213–220. https://doi.org/10.1016/j.thromres.2004.06.007

Yana, N. T. Y., Shipon, M. N. H., Bristy, A. H., Safa, F. A., Hossain, M. A., & Al Hasan, M. S. (2025). Carnosic Acid as a Promising Anticancer Agent: Mechanisms of Action and Therapeutic Potential Across Multiple Cancer Types. *Journal of Chemistry Insights and Discoveries*, 1(01), 1-5. https://doi.org/10.71193/jcid.20250001

Zhang, X. A., Zhang, S., Yin, Q., & Zhang, J. (2015). Quercetin induces human colon cancer cells apoptosis by inhibiting the nuclear factor-kappa B Pathway. *Pharmacognosy magazine*, *11*(42), 404–409. https://doi.org/10.4103/0973-1296.153096