

Review Article

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Cell Cultures as a Platform for Optical Diagnostics and Toxicological Analysis: Cancer Predictors and Cytotoxicity of Organic Compounds

This review examines the use of cell cultures as an experimental platform for optical diagnostics and the assessment of the cytotoxic effects of organic compounds. *In vitro* models, including primary cell cultures, immortalized cell lines, and tumor cell lines, are used to investigate biochemical changes associated with malignant transformation and cytotoxic effects. Particular emphasis is placed on Raman and infrared spectroscopy as label-free methods for detecting molecular alterations and evaluating dose-dependent cellular responses to organic compounds. The review covers studies using human cell lines, including MCF-7, HeLa, A549, HepG2, HL-60, and U-937, with particular attention to documented changes in lipid and protein composition, structural abnormalities, and metabolic adaptations. The integration of cellular models with optical methods enables the acquisition of reproducible and quantitatively measurable indicators of biochemical changes, thereby supporting the development of novel diagnostic approaches and the assessment of compound toxicity. The findings highlight the scientific value of cell cultures as a versatile platform for both fundamental and applied research in oncology and toxicology.

Keywords: cell cultures, cytotoxicity, organic compounds, Raman spectroscopy, infrared spectroscopy, optical diagnostics, *in vitro*.

Introduction

Cell cultures are widely employed as experimental tools in applied, fundamental, and biological research, representing one of the principal *in vitro* models [1]. They are valued for being convenient and readily controllable systems [2], enabling the study of cellular structural, functional, and metabolic features under both normal and pathological conditions [3]. Additionally, *in vitro* cultures allow the assessment of various chemical and physical factors within precisely defined experimental settings [4].

Due to their ease of cultivation and high reproducibility, cell cultures are widely used in oncology, toxicology, and pharmacology [5]. They offer a convenient experimental platform for controlled *in vitro* studies. Cell cultures are frequently used to investigate cellular mechanisms, assess the toxicity of substances, and prescreen potentially effective compounds [6, 7].

In recent years, the application of cell cultures in combination with optical research methods has gained particular relevance. Optical microscopy, along with fluorescent and spectroscopic techniques, enables the monitoring of changes in cell morphology, structure, and biochemical state without disrupting the sample [8, 9]. These capabilities make such methods promising for the early detection of malignant cell transformation, as well as for evaluating the cytotoxic effects of various organic compounds at the cellular level [10].

Scientific literature reports various findings on the use of cell cultures in oncological research and toxicological analysis. These studies demonstrate optical methods are applied to both tumor and non-tumor cell lines to study cellular changes and assess the various chemical compounds toxicity [11–13]. At the same time, various publications consider these aspects separately, focusing either on the cell cultures biological characteristics or on individual optical methods without a comprehensive examination [14, 15]. This indicates the relevance of using cell culture analysis as a unified experimental platform for optical diagnostics and toxicological assessment.

A key issue in this field is the lack of a comprehensive understanding of the capabilities and limitations of using cell cultures to identify optical predictors of malignant transformation and to assess the cytotoxic effects of organic compounds. The criteria for interpreting optical data obtained from cell models, as well as their relevance to preclinical research, remain insufficiently defined [16].

The object of this study is cell cultures employed in biomedical research, while the subject is their application in optical diagnostics of malignant transformations and the toxicological assessment of organic compounds. The aim of this review article is to analyze and systematize the scientific literature on the use of cell cultures as a platform for optical diagnostics and toxicological evaluation. To achieve this goal, the article addresses the following objectives: to review the main types of cell cultures and their applications; to analyze the advantages and limitations of cell cultures as *in vitro* models; to describe the optical methods employed to study cell cultures in oncology.

Experimental

A systematic approach was employed to analyze the scientific literature for this review. The primary sources of information included the international databases PubMed, Web of Science, and Scopus, as well as open-access scientific journals publishing research in the fields of cell biology, oncology, toxicology, and spectroscopy. Inclusion criteria encompassed studies focused on the use of cell cultures (primary, immortalized, and tumor cell lines) as models for investigating biochemical changes associated with malignant transformation and the cytotoxicity of organic compounds, as well as studies employing spectroscopic methods for the quantitative and qualitative analysis of cellular components. Studies lacking experimental data or without a detailed description of spectroscopic methods were excluded. Data were systematically organized to analyze cell line types, studied compounds, applied spectroscopic approaches (Raman and FTIR), and identified biochemical changes. The collected materials were used to summarize current trends, compare results across studies, and highlight prospects for the development of optical diagnostics and *in vitro* toxicological analysis.

Main types of cell cultures and their applications

Cell cultures are experimental systems consisting of populations of cells maintained outside the organism under controlled *in vitro* conditions. Such conditions ensure cell viability, support proliferation, and preserve essential biological functions. Consequently, cell cultures are widely used as model systems for the investigation of cellular processes, the study of pathological alterations, including malignant transformation, and the assessment of the cytotoxic effects of chemical compounds [17, 18].

Cell cultures are classified into three main types based on their source and biological characteristics: primary cultures, immortalized cell lines, and tumor cell lines [19, 20].

Primary cell cultures are obtained directly from body tissues and maintained *in vitro* without prolonged adaptation or targeted genetic modification. As a result, they largely preserve the morphological, functional, and metabolic characteristics of the original tissue, including specific cellular phenotypes and regulatory mechanisms [21]. For example, primary human mammary epithelial cells (HMECs) have been isolated and cultured from mammary tissue to study fundamental aspects of breast biology and diseases, including early stages of breast cancer development [22]. Primary human hepatocytes isolated from resected liver tissue are frequently used as physiologically relevant models to study drug metabolism, cytochrome P450 regulation and response to xenobiotics *in vitro* [23]. Similarly, primary adult cardiomyocytes isolated from human myocardium were cultured to evaluate electrophysiological properties and cardiotoxic responses to therapeutic compounds, demonstrating their utility in cardiovascular research and drug safety assessment [24]. Their close resemblance to native tissue underlies their high biological relevance, making primary cultures an important tool in fundamental research [25]. They are widely employed to investigate cellular mechanisms underlying tumor development, to study disruptions in cellular regulation [26], and to experimentally assess the effects of various chemical compounds at the cellular level [27].

Immortalized cell lines are characterized by their ability to undergo an unlimited number of cell divisions, making them a convenient and stable platform for long-term, reproducible experiments. This enables the standardization of experimental conditions and the comparability of results across different studies. For example, the Jurkat T-lymphoblastic cell line, derived from human T-lymphoblastic leukemia, is routinely used in an *in vitro* model to study signaling pathways during T-cell activation and their functional roles, in-

cluding studies of T-cell receptor (TCR) signaling pathways and cytokine production in response to stimulation protocols [28]. Similarly, the HEK293 cell line, an immortalized human kidney cell line, is commonly used as a host system for transient expression studies, recombinant protein production, and viral vector production due to its high transfection and robust growth properties [29]. Immortalized hepatoma cell lines, such as Huh7 cells play a key role in virological research as they enable efficient replication of hepatitis C virus (HCV) RNA in culture and allow the screening of antiviral compounds that would otherwise be difficult to evaluate in primary hepatocyte systems [30]. Their role as model systems for studying the molecular mechanisms of cell activity, analyzing signaling pathways, and performing pharmacological and toxicological screening of various compounds confirms their importance for basic and applied research. Immortal cell lines also play a key role in the development and validation of cell-model-based diagnostic methods, such as reporter assays generated on transformed cell lines to detect biomarker-mediated responses [31].

Tumor cell lines are derived from malignant neoplasms of various origins. Their distinguishing feature is the disruption of growth, proliferation, and cell cycle regulation, which makes them a valuable tool for studying tumor cell biology [32]. For example, human breast adenocarcinoma MCF-7 and hepatocellular carcinoma HepG2 cell lines are frequently used in cancer research to study metabolic changes and stress responses in tumor cells; studies have shown how metabolic inhibition and hypoxic conditions affect viability and apoptotic markers in these tumor cell lines, providing insight into regulatory pathways associated with carcinogenesis [33]. In another study, a range of human ovarian tumor cell lines, including IGROV1, OVCAR-3, OVCAR-4, OVCAR-5, OVCAR-8, and SK-OV-3, were used to characterize the antitumor activity of the chemotherapeutic agent irifolven. Significant antiproliferative effects were demonstrated *in vitro*, and the suitability of these cell lines for the preclinical evaluation of cytotoxic compounds was confirmed [34]. The human cervical cancer cell line HeLa is derived from a malignant epithelial tumor. Fourier-transform infrared spectroscopy (FTIR) and Raman spectroscopy were used to investigate changes in the protein and lipid composition of HeLa cells following cytotoxic and pharmacological stimulation. For example, FTIR and Raman imaging of HeLa cells treated with the adaptogen withaferin A revealed dose-dependent biochemical changes in lipid-related spectral regions and protein secondary structures. This suggests alterations in cellular metabolism and response to chemical substances [35]. Further studies demonstrated that cell cycle-dependent changes in the FTIR spectra of HeLa cells correlate with changes in amide I and II bands, which are associated with protein conformation and cell state [36]. Raman spectroscopy combined with atomic force microscopy was also used to detect changes in the DNA, lipid, and protein composition of HeLa cells after exposure to external substances such as nanoparticles. This confirmed that the vibrational signatures reflect molecular adaptation to the treatment [37]. These studies demonstrate the suitability of HeLa cells for assessing cytotoxic effects and for investigating biochemical reactions in solid tumor models using optical methods.

In contrast, the human leukemia cell lines HL-60 and U-937 are derived from hematological malignancies and grow in suspension, making them suitable models for toxicological and spectroscopic investigations. Leukemia cell cultures have been extensively studied using Raman spectroscopy and Fourier-transform infrared spectroscopy (FTIR) to identify alterations in protein, lipid, and nucleic acid composition associated with cytotoxic effects and apoptosis [38, 39]. The combined use of solid tumor and leukemia cell lines allows for a comparative evaluation of cytotoxic effects and molecular reactions in different cancers using optical spectroscopic methods.

Tumor cell lines of various origins are frequently used to model solid and hematological malignancies *in vitro*. These lines are employed to investigate the mechanisms of carcinogenesis, analyze the phenotypic and molecular characteristics of malignant cells, and identify potential cellular markers of tumor transformation. In applied research, such cultures are used to assess antitumor activity and the cytotoxic effects of organic compounds using various analytical techniques, including optical methods, which provide information on structural, functional, and biochemical changes in cells [40].

Cell cultures as an experimental model in vitro: advantages and limitations

Cell cultures are regarded as a common *in vitro* model in biomedical research, owing to the ability to maintain strict control over experimental conditions and achieve highly reproducible results when studying cellular processes. The use of cell cultures enables the analysis of the effects of various factors on cells under standardized conditions, which is particularly important for oncology and toxicology studies [41].

The main advantages of cell cultures are the strict control of experimental conditions, including the composition of the culture medium, the concentration of the compounds being studied, the temperature, and the exposure time. These conditions ensure reproducible results and enable quantitative analysis of cellular responses. Moreover, cell cultures offer high experimental flexibility, enabling the variation of study parameters and the modeling of diverse biological conditions.

A significant benefit of cell models is the ability to investigate cellular mechanisms at the molecular and subcellular levels [42]. The use of cell cultures facilitates the analysis of proliferation, apoptosis, metabolic changes, and the structural organization of cells. This makes them indispensable for studies of carcinogenesis as well as for assessing the cytotoxic effects of chemical compounds [43].

Despite their advantages, cell cultures as *in vitro* models have several limitations. One limitation is the simplified nature of the system compared to *in vivo* conditions, as cell cultures do not fully reflect complex intercellular and tissue interactions, nor the influence of systemic factors present in the organism. This restricts the direct extrapolation of results to whole-organism contexts [44]. Another limitation is the variability of cellular characteristics during long-term culture, particularly for immortalized and tumor cell lines. Such changes can affect morphology, metabolism, and gene expression, which must be considered when interpreting results. Additionally, study outcomes may depend on the specific cell line used and the culture conditions applied [45].

Cell cultures represent an effective and informative *in vitro* model with several significant advantages, but careful interpretation of data and consideration of their limitations are essential.

Optical methods for the identification of cancer-related predictors in cell cultures

Optical spectroscopic techniques are widely applied to examine molecular changes associated with tumor phenotypes and are recognized as effective tools for identifying cancer-related predictors *in vitro*. By analyzing the spectral properties of cell cultures, researchers can detect variations in biochemical composition corresponding to different levels of malignancy and tumor aggressiveness. Among these methods, Raman and infrared (IR) spectroscopy stand out in oncology research due to their label-free operation and high molecular specificity. For example, investigations of urothelial carcinoma cell lines, including T24a, T24p, RT4, HT-1376, and J82, using both Raman and FTIR imaging, have revealed that the spectral signatures reflect critical molecular differences between malignant and non-malignant cells, correlating with malignancy grade and invasive potential. These findings support the use of such spectroscopic profiles as reproducible indicators of cancer-related molecular changes *in vitro* [46]. The use of well-characterized tumor cell lines provides a controlled experimental platform for correlating spectral signatures with specific malignant phenotypes, facilitating the identification of reproducible molecular predictors of cancer development [47].

Raman spectroscopy is widely applied to characterize the biochemical profiles of tumor cell lines and to distinguish them from less aggressive cellular models. Studies involving breast cancer cell lines such as MDA-MB-231, MDA-MB-468, HCC-1143, and MCF-7 have demonstrated that both Raman and infrared spectral analyses can reveal molecular features characteristic of distinct tumor subtypes. In these models, Raman spectra have been shown to reflect differences in cellular lipid organization, protein secondary structure, and nucleic acid content, which are associated with variations in tumor aggressiveness. Such spectral distinctions enable the differentiation of highly invasive cell lines from less aggressive ones, supporting the use of Raman-based molecular fingerprints as potential predictors of tumor behavior [48].

Several studies have shown that Raman spectroscopy is sensitive to biochemical adaptations and metabolic features of tumor cells [49]. For instance, comparative analyses of the MDA-MB-231 and MCF-7 cell lines indicate that the intensity of spectral bands associated with lipid and protein components correlates with cellular aggressiveness and metastatic potential. In these investigations, elevated lipid-associated Raman signals were linked to increased membrane remodeling and altered energy metabolism in more aggressive cells. The application of multivariate statistical methods, including principal component analysis (PCA), allows the identification of informative spectral features and facilitates reliable discrimination between tumor cell lines [50]. As a result, cell line-specific spectral profiles can be generated and further explored as quantitative predictors of malignant phenotype and progression.

Infrared spectroscopy, particularly Fourier-transform infrared (FTIR) spectroscopy, complements Raman analysis by detecting the absorption of infrared radiation by specific molecular functional groups [51]. Studies of tumor cell lines have shown that alterations in amide I and amide II bands, as well as lipid-

associated spectral regions, reflect biochemical shifts characteristic of malignant transformation. Using breast cancer cell lines such as MCF-7 and more aggressive counterparts, FTIR spectroscopy has been shown to detect differences in protein-to-lipid ratios and conformational changes in cellular macromolecules. These FTIR-derived spectral features provide reproducible indicators of tumor-associated biochemical remodeling and can be employed to distinguish cell populations with different malignant potentials [52].

Overall, the application of Raman and infrared spectroscopic techniques to cell cultures enables the detection of stable molecular changes associated with tumor development. The resulting spectral profiles reflect key biochemical characteristics of malignant cells, including alterations in lipid metabolism, protein structure, and nucleic acid content, and may be considered potential predictors of cancer. Consequently, cell cultures serve as an effective and informative experimental platform for the development and validation of optical diagnostic approaches aimed at identifying cancer-related predictors in oncology research [53].

Cell cultures as a model for the assessment of cytotoxicity of organic compounds using optical methods

Cell cultures are widely used in toxicological studies to assess the cytotoxic effects of organic compounds, as they allow for the direct analysis of chemical impacts on cells derived from various tissues under controlled conditions [54]. In such studies, Raman and infrared spectroscopy are applied as optical techniques for detecting biochemical alterations in cells induced by toxic agents without the use of labels or destructive sample preparation [55].

Liver cell lines, particularly HepG2, are among the most commonly used models for evaluating the cytotoxicity of organic compounds with potential hepatotoxic effects. Several studies employing this model have investigated the impact of organic solvents, such as dimethylformamide and ethanol, as well as aromatic hydrocarbons and pharmacologically active compounds [56, 57]. Exposure to these substances induces alterations in lipid and protein components of HepG2 cells, which can be detected in both Raman and FTIR spectra. Spectral features associated with membrane integrity disruption and metabolic dysfunction have been shown to correlate with reduced cell viability, allowing these changes to be considered indicators of cytotoxic effects [58].

The HeLa and A549 cell lines are widely used in studies aimed at assessing the cytotoxicity of organic compounds in epithelial cells. In HeLa cells, Fourier-transform infrared (FTIR) spectroscopic analysis has been applied to detect biochemical changes in protein and lipid regions following exposure to pharmacologically active and toxic agents [59]. FTIR spectra of HeLa cells reveal alterations in amide I/II bands and lipid-related regions corresponding to cellular responses, including cell cycle arrest and phenotypic changes induced by external compounds [60]. Raman spectroscopy has also been successfully applied to live HeLa cells, demonstrating that vibrational signatures can provide detailed molecular information (including lipids and proteins) when HeLa cells are examined under different experimental conditions [61]. In A549 models, FTIR spectroscopy has been used to monitor apoptosis and cytotoxicity induced by toxic agents, including predominantly organic compounds as well as inorganic toxicants such as arsenic trioxide, demonstrating shifts in spectral regions associated with proteins, lipids, nucleic acids, and carbohydrates [62]. The combined application of Raman and infrared spectroscopy enables a more comprehensive characterization of cellular responses to toxic exposure, revealing complementary biochemical insights into membrane integrity, protein conformation, and metabolic dysfunction.

The MCF-7 breast cancer cell line is frequently employed to evaluate the cytotoxicity of organic anti-tumor compounds, natural bioactive substances, and synthetic organic molecules considered as potential therapeutic agents. In such studies, Raman and FTIR spectroscopy have been used to detect changes in the protein and lipid composition of cells, reflecting structural damage and disturbances in cellular energy metabolism [63]. The resulting spectral data have been applied for the comparative assessment of toxic effects and for the analysis of dose-dependent cellular responses [64].

In a number of studies, cell cultures have been used to construct dose-dependent models of cytotoxicity for organic compounds of various chemical classes, including aromatic compounds, alcohols, ketones, and pharmacologically active molecules. The use of a single cell line in combination with Raman and infrared spectroscopy allows the generation of reproducible spectral profiles that reflect the extent of cellular damage at different toxicant concentrations [65, 66]. These spectral profiles complement conventional cell viability assays and can be employed for the quantitative evaluation of cytotoxic effects *in vitro*.

The main cell lines, studied compounds, and applied spectroscopic methods are summarized in Table 1.

Application of cell lines and optical methods in cytotoxicity studies

Cell line	Type of organic compounds	Method	Main detected changes	References
HepG2	Organic solvents, aromatic compounds	Raman, FTIR	Changes in lipid and protein components	[67]
HeLa	Pharmacologically active compounds	Raman, FTIR	Shifts in amide bands and lipid regions	[68]
A549	Toxic organic compounds	FTIR	Apoptosis-associated spectral changes	[62]
MCF-7	Organic antitumor compounds	Raman, FTIR	Protein-lipid balance disorders	[69]

Thus, the integration of cell culture models with Raman and infrared spectroscopy represents an effective platform for assessing the cytotoxicity of organic compounds [66]. This approach enables the identification of molecular and biochemical changes induced by toxic exposure and supports the use of spectral characteristics for the comparative analysis and evaluation of the potential toxicity of organic substances [69].

Conclusion

The review demonstrates cell cultures serve as a versatile platform for research in optical diagnostics and toxicological analysis. The use of primary, immortalized, and tumor cell lines allows for the reproducible assessment of biochemical and structural changes resulting from both malignant transformation and exposure to organic compounds. Application of Raman and infrared spectroscopy facilitates the identification of molecular cancer markers, structural alterations in proteins and lipids, and cellular metabolic adaptations. The compiled data confirm the effectiveness of cell models for both quantitative and qualitative analysis of biochemical processes, as well as their potential in the development of new diagnostic approaches and the *in vitro* assessment of compound toxicity. Future research should focus on standardizing spectroscopic analysis methods and expanding the use of cell models for the predictive evaluation of biochemical and pharmacological effects of substances.

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**Жасуша өсіндісі оптикалық диагностика
және токсикологиялық талдау платформасы ретінде:
қатерлі ісік предикторлары және органикалық
қосылыстардың цитотоксикалық әсері**

Шолу мақалада жасуша өсіндісін оптикалық диагностика және органикалық қосылыстардың цитотоксикалық әсерін бағалау үшін эксперименттік платформа ретінде пайдалану қарастырылған. Қатерлі трансформациямен және уытты әсерлермен байланысты биохимиялық өзгерістерді зерттеу үшін бастапқы өсіндісі, сондай-ақ өлмейтін және ісік жасуша желілерін қоса алғанда, *in vitro* модельдері қолданылды. Молекулалық өзгерістерді анықтау және органикалық қосылыстарға дозаға тәуелді жасушалық реакцияларды бағалау үшін таңбасыз әдістер ретінде Раман және инфрақызыл спектроскопияға ерекше назар аударылды. Қарастырылған зерттеулер липидтер мен ақуыз құрамының құжатталған өзгерістеріне, құрылымдық ауытқуларға және метаболикалық бейімделулерге назар аудара отырып, MCF-7, HeLa, A549, HepG2, HL-60 және U-937 сияқты адам

жасуша желілерін қамтиды. Жасуша модельдерін оптикалық әдістермен біріктіру биохимиялық өзгерістердің қайталанатын және сандық тұрғыдан маңызды көрсеткіштерін алуға мүмкіндік жасайды, бұл жаңа диагностикалық тәсілдерді әзірлеу және қосылыстың уыттылығын бағалау үшін мүмкіндіктер береді. Қорытындыда жасуша өсімдісінің онкология мен токсикологиядағы іргелі және қолданбалы зерттеулер үшін жан-жақты платформа ретіндегі ғылыми құндылығы атап өтілген.

Кілт сөздер: жасуша өсімдісі, цитотоксикалық әсер, органикалық қосылыстар, Раман спектроскопиясы, инфракызыл спектроскопия, оптикалық диагностика, *in vitro*.

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Культуры клеток как платформа для оптической диагностики и токсикологического анализа: предикторы рака и цитотоксичность органических соединений

В данной обзорной статье мы рассматриваем использование клеточных культур в качестве экспериментальной платформы для оптической диагностики и оценки цитотоксического действия органических соединений. Для исследования биохимических изменений, связанных со злокачественной трансформацией и токсическим действием, используются модели *in vitro*, включая первичные культуры, а также иммортализованные и опухолевые клеточные линии. Особое внимание уделяется рамановской и инфракрасной спектроскопии как безметочным методам обнаружения молекулярных изменений и оценки дозозависимых клеточных ответов на органические соединения. Рассмотренные исследования включают клеточные линии человека, такие как MCF-7, HeLa, A549, HepG2, HL-60 и U-937, с акцентом на документированные изменения в липидном и белковом составе, структурные аномалии и метаболические адаптации. Интеграция клеточных моделей с оптическими методами позволяет получать воспроизводимые и количественно значимые показатели биохимических изменений, предоставляя возможности для разработки новых диагностических подходов и оценки токсичности соединений. В выводах подчеркивается научная ценность клеточных культур как универсальной платформы для фундаментальных и прикладных исследований в онкологии и токсикологии.

Ключевые слова: клеточные культуры, цитотоксичность, органические соединения, рамановская спектроскопия, инфракрасная спектроскопия, оптическая диагностика, *invitro*.

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