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Pharmacological and Pharmaco-economical aspect of Huh7 cell line

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Abstract
A popular *in vitro* model for liver research, the Huh7 cell line is derived from a human hepatocellular carcinoma and has characteristics similar to those of hepatocytes, such as the synthesis of albumin, metabolic activity and lipid processing. In virology and the development of antiviral drugs, Huh7 cellswhich were first created in 1982are particularly prized for their high permissiveness to hepatotropic viruses such as HCV and HBV. They also perform as reliable models for steatotic liver disease (MASLD) linked to metabolic dysfunction, reproducing steatosis by exposure to fatty acids and facilitating research on inflammation, oxidative stress, lipid metabolism and mitochondrial dysfunction. Huh7 cells have great transfection effectiveness, reproducible results and adaptability for long-term, high-throughput pharmacological screening, despite drawbacks such aberrant gene expression and fluctuating enzyme levels. Their contributions to the understanding of autophagy modulation, antioxidant treatments and drug-induced liver injury (DILI) pathways have been crucial. Additionally, the cell line is useful for pharmacogenomic and nutraceutical research, helping to identify molecular targets and assess phytochemicals such as resveratrol, curcumin and quercetin. Huh7 cells is a more affordable, scalable and genetically adjustable system than other cell lines (such as HepG2, CHO, HEK293, Caco-2 and PHH) for drug discovery, gene regulation research and precision medicine techniques in liver-specific pharmacology and toxicology.

Keywords: Huh7 cell line, MASLD, drug-induced liver injury, pharmacogenomics, antiviral and antioxidant drug screening

Introduction

Huh7 Cell Line

The Huh7 cell line is a human hepatocellular carcinoma (HCC) derived cell line that has become one of the most extensively utilized *in vitro* models for liver-based research. Originally established in 1982 by Nakabayashi and colleagues from a liver tumour biopsy of a 57-year-old Japanese male. Huh7 cells exhibit many hepatocyte-like properties, including albumin production, metabolic enzyme activity and lipid-processing capabilities (Nakabayashi *et al*., 1982) [15]. These characteristics make them a preferred model for studying liver physiology, hepatocellular carcinoma mechanisms and drug-induced hepatotoxicity.

One of the most defining features of Huh7 cells is their high permissiveness to hepatotropic viruses, particularly the hepatitis-C virus (HCV). This unique susceptibility has made them indispensable for virology research, especially in the development of the HCV replicon system and full-length infectious models, which have revolutionized antiviral drug discovery (Blight *et al*., 2002) [1]. In contrast to primary human hepatocytes, which are limited by donor variability and short-term viability, Huh7 cells offer a stable, reproducible and long-term culture platform with consistent genetic background, making them suitable for high-throughput screenings. Beyond virology, Huh7 cells have gained traction in metabolic liver disease modelling, particularly in the context of metabolic dysfunction-associated steatotic liver disease (MASLD), previously known as non-alcoholic fatty liver disease (NAFLD).

Upon exposure to free fatty acids such as palmitic or oleic acid, Huh7 cells accumulate lipid droplets within the cytoplasm, mimicking hepatic steatosis. This lipid-laden phenotype facilitates the study of lipid metabolism, oxidative stress, mitochondrial dysfunction and insulin resistance, which are key components in MASLD pathogenesis (Castell *et al*., 2020) [2]. Their ability to model steatosis also makes them suitable for evaluating the therapeutic potential of antisteatotic and antioxidant compounds *in vitro*.

In addition to their hepatocytic traits, Huh7 cells exhibit features of cancer cells, such as aneuploidy, loss of contact inhibition and continuous proliferation. While this immortalization supports ease of culture and long-term experiments, it also introduces limitations. These include aberrant gene expression compared to normal hepatocytes, altered drug-metabolizing enzyme levels, and reduced expression of certain liver-specific proteins (Wilkening *et al*., 2003) [24]. Therefore, while Huh7 cells are highly valuable, their limitations must be considered when extrapolating *in vitro* findings to *in vivo* systems or clinical settings.

Recent advancements in gene editing and transcriptomic profiling have further enhanced the utility of Huh7 cells. Researchers are now using CRISPR-Cas9 and RNA sequencing technologies to modify specific pathways, identify gene targets and better understand the molecular basis of liver diseases and liver cancer. Furthermore, Huh7 cells can be transfected with reporter constructs, viral genomesor plasmids encoding genes of interest, allowing dynamic investigation of intracellular signaling, inflammation, autophagy and apoptosis (Sainz *et al*., 2006) [17].

Huh7 Cell Line

Development of differentiated human hepatoma cell lines in chemically defined media

This ground-breaking study created the Huh7 cell line from a hepatocellular carcinoma that had undergone good differentiation. It proved that Huh7 cells could maintain essential hepatic processes *in vitro*, including the expression of metabolic enzymes and albumin secretion. This study established the foundation for the use of Huh7 cell as a repeatable and dependable model in drug metabolism investigations, liver disease research, and antiviral screening, specifically for the hepatitis-C virus (HCV). For scholars looking into pharmaco-toxicology, hepatocarcinogenesis and liver physiology, it continues to be one of the most often mentioned sources (Nakabayashi *et al*., 1982) [15].

Hepatitis-C Virus RNA replication employing highly permissive cell lines for sub-genomic and genomic replication

This seminal work showed that Huh7 cells could sustain robust replication of HCV, RNA using both sub-genomic and full-length replicons. By offering the first effective *in vitro* system for examining viral replication, life cycle and host-virus interactions, it completely changed the field of HCV research. Since then, the work has revolutionised the treatment of HCV by directly facilitating the development and screening of direct-acting antivirals (DAAs). Huh7 cells is now at the forefront of antiviral medication development for liver-targeting viruses after this study confirmed its importance as a model for viral pharmacology, virology research and therapeutic discovery (Blight *et al*., 2002) [1].

Comparison of the biotransformation properties of primary human hepatocytes and the Hepatoma Cell Line HEPG2

This study is important for comprehending the metabolic competence of hepatoma cell lines, including Huh7 cells, even though it mainly compares HepG2 with primary hepatocytes. It draws attention to the drawbacks and benefits of using transformed cell lines in research on drug metabolism. In hepatoma-derived models such as Huh7 cells, the study offers a standard for assessing cytochrome P450 expression and biotransformation ability. According to (Wilkening *et al*., 2003) [24], this has helped researchers choose and genetically change Huh7 cells for pharmacokinetic and hepatotoxicity investigations, confirming their value as an affordable substitute for primary hepatocytes in early-stage drug screening.

Finding a novel Hepatitis-C virus entry factor

Using Huh7 cells, this research discovered Niemann-Pick-C1 (NPC1) to be an essential receptor for HCV entrance. It emphasised Huh7 cells as the perfect instrument for analysing the molecular mechanisms of viral entry and broadened our knowledge of host-virus interactions. The study identified novel treatment targets for viral suppression in addition to offering insights into the pathophysiology of HCV. This study validated Huh7 cells as a reliable system for assessing viral entry inhibitors and host-specific pathways in liver-targeted diseases and further supported its function in antiviral pharmacology, particularly in screening for host-targeting agents (Sainz *et al*., 2006) [17].

In vitro models for the study of drug-induced hepatotoxicity and liver diseases

This review focusses on a number of *in vitro* hepatic models, such as Huh7 cells, for the study of drug-induced hepatotoxicity and liver diseases. It highlights the value of Huh7 cells in simulating inflammation, oxidative stress and steatosis, particularly in fatty acid-induced environments that resemble MASLD. The study confirms the usefulness of Huh7 cells in pharmacological screens for antioxidant, hepatoprotective and antisteatotic substances. It also covers changes like co-culturing and genetic engineering that improve their metabolic performance. For drug development and toxicity testing, especially in metabolic and liver disease, this reference highlights Huh7 cells as a viable and easily available substitute for primary hepatocytes (Castell *et al*., 2020) [2].

Neutrophil depletion prevents acetaminophen hepatotoxicity in mice

Although this seminal study was carried out *in vivo*, it is frequently referenced in *in vitro* hepatotoxicity studies that employ models such as Huh7 cells. Using Huh7 cells as a model, it investigates the roles of oxidative stress, mitochondrial dysfunction and inflammatory signalling in acetaminophen-induced liver damage. The results have influenced the pharmacological evaluation of antioxidants and hepatoprotective substances in systems based on Huh7 cells. Huh7 cells have subsequently been employed to research acetaminophen-induced cytotoxicity, ROS production and mitochondrial collapse, making them

excellent for screening antidotes or protective drugs in DILI-related pharmacology (Liu *et al*., 2006) [13].

The role of oxidative stress in the development of steatohepatitis in a rat model

Despite being based on an animal model, this study is extremely pertinent to *in vitro* steatosis research employing Huh7 cells because it examines the role of oxidative stress in the development of steatohepatitis in a rat model. It illustrated how oxidative stress contributes to the development of steatohepatitis from hepatic steatosis, a phenomenon commonly confirmed in MASLD models based on Huh7 cells. Researchers can mimic this pathogenic shift by using free fatty acids to induce oxidative stress in Huh7 cells. This allows for the pharmacological assessment of anti-inflammatory and antioxidant drugs. According to (Yanagimoto *et al*., 2004), the study backs up the use of Huh7 cells as a trustworthy system to test therapeutic interventions meant to mitigate oxidative liver damage and to model the early progression of MASLD.

***In vitro* assessment of liver-specific functionalities using hepatoma cell lines Hepg2 and Huh7 Cells**

This work directly analyses the hepatic functioning of two common hepatoma cell lines, HepG2 and Huh7, in terms of their suitability for *in vitro* pharmacological testing. It draws attention to the fact that Huh7 cells show higher expression of particular liver-specific markers, such as phase I/II detoxification and lipid metabolism-related enzymes. These results support the applicability of Huh7 cells for modelling metabolic liver disorders, drug metabolism and hepatotoxicity screening. In keeping with the 3Rs (Replacement, Reduction, Refinement) in preclinical pharmacology, the study also advocates for the incorporation of Huh7 cells into alternative testing methodologies, which lessen the need for animal models (Schulze *et al*., 2009) [18].

RNA replication and virion production in hepatitis-b virus infected Huh7 Cells

This study expanded the Huh7 cells virological utility to include hepatitis-B virus (HBV) in addition to hepatitis-C virus (HCV). The scientists showed that when transfected with replicationcompetent viral DNA, Huh7 cells promote HBV replication and virion generation. This groundbreaking study increased the function of Huh7 cells in hostpathogen interaction research and antiviral medication screening for HBV, a leading cause of liver disease worldwide. Additionally, it validated the cell lines utility for testing antiviral drugs and comprehending liverspecific viral life cycles, confirming its adaptability for pharmacological investigations targeting DNA and RNA viruses (Shlomai *et al*., 2008) [19].

Resveratrol's anti-steatotic and anti-inflammatory actions in Huh7 cells treated with oleic acid

This work shows how using Huh7 cells to simulate fatty acid-induced steatosis and assess medicinal medicines like resveratrol may be a successful approach. In Huh7 cells exposed to oleic acid, a common MASLD model, the authors demonstrated that resveratrol significantly decreased lipid accumulation and inflammatory gene expression. This study highlights how Huh7 cells is a useful tool in metabolic pharmacology for screening natural compounds with anti-lipogenic and antioxidant qualities. Additionally, it offers a uniform platform for investigating nutraceutical treatments for liver conditions such as steatohepatitis and MASLD (Choi *et al*., 2015) [4].

Huh7 cells as a model for assessing the hepatoprotective activity of phytochemicals

This study emphasises the use of Huh7 cells to evaluate the hepatoprotective potential of phytochemicals, especially under conditions of oxidative and steatotic stress. The scientists used cytotoxicity, lipid accumulation and ROS tests to expose Huh7 cells to recognised hepatotoxins and evaluate the protective effects of plant-derived chemicals. Their findings confirmed that Huh7 cells is a dependable system for screening natural compounds and researching mechanisms of action. The study encourages the development of plant-based treatments for liver disorders such as MASLD and drug-induced liver injury (DILI) by endorsing the use of the cell line in ethnopharmacology and alternative medicine research (Gupta *et al*., 2014) [6].

Assessment of mitochondrial dysfunction in Huh7 cells exposed to hepatotoxic medicines

This investigation assessed the detrimental effects of hepatotoxic pharmaceuticals, such as troglitazone and acetaminophen, on the mitochondria of Huh7 cells. To evaluate cellular bioenergetics, the scientists assessed ROS generation, ATP synthesis and mitochondrial membrane potential. According to their research, Huh7 cells are very vulnerable to mitochondrial damage, which makes them a useful model for early detection of mitochondrial toxicitya crucial factor in assessing the safety of drugs. According to (Wang *et al*., 2012), this result supports the use of Huh7 for mechanistic toxicity research, particularly when examining drug-induced oxidative stress, mitochondrial dysfunction and hepatocyte death.

Protective effects of curcumin against oxidative stress and lipid accumulation caused by free fatty acids in Huh7 Cells

This study examined the protective effects of curcumin, a naturally occurring antioxidant, against oxidative stress and lipid accumulation caused by oleic acid in Huh7 cells. The findings demonstrated that curcumin dramatically lowered intracellular triglyceride levels and oxidative stress indicators, demonstrating its promise as an antisteatotic and hepatoprotective drug. This study confirms that Huh7 cells are a valid *in vitro* model for oxidative liver injury and MASLD, particularly for the screening of compounds derived from plants. It emphasises how beneficial Huh7 cells is for pharmacological studies that focus on inflammation, lipid metabolism and antioxidant treatments (Chen *et al*., 2013) [3].

Gpnmb and Activin-A mediate protective effects in MASLD Models

This current work uses Huh7 cells and *in vivo* models to investigate the protective functions of Gpnmb and Activin-A in metabolic dysfunction-associated steatotic liver disease (MASLD). Overexpression of these molecules dramatically decreased oxidative stress and lipid accumulation in Huh7 cells under steatogenic conditions. The results imply that Gpnmb and Activin-A function as endogenous defence factors in hepatocytes, providing novel pharmaceutical

targets for the therapy of MASLD. In metabolic liver illnesses, our result supports the use of Huh7 cells as a translational model to find therapeutic regulators of lipid metabolism and liver inflammation (Zhou *et al*., 2024) [29].

Screening of Antidiabetic compounds using Huh7 cells expressing human insulin receptor

This study employed genetically modified Huh7 cells expressing the human insulin receptor to screen for compounds with potential antidiabetic effects. The scientists showed that Huh7 cells may function as a sensitive and responsive hepatocyte-based system for examining insulin resistance and how therapeutic drugs can modulate it by assessing glucose uptake and insulin signalling pathways. The model is especially pertinent for pharmacological research in type-2 diabetes, MASLD and metabolic syndrome as it offered a useful platform for examining hepatic glucose metabolism and screening insulin-sensitizing substances. According to (Zhang *et al*., 2017) [28], it also demonstrated Huh7 cells versatility for receptor-specific tests.

The effects of oestrogenic substances on hepatic lipid metabolism

This research examined the effects of oestrogenic substances on hepatic lipid metabolism using Huh7 cells as a model to evaluate oestrogenic regulation of lipid metabolism. The scientists demonstrated how exposure to xenoestrogens and 17β-oestradiol altered steatosis-related metabolic pathways, gene expression and lipid accumulation. The results demonstrate Huh7 cells endocrine responsiveness, confirming its use in evaluating hormone-related metabolic impacts and identifying possible endocrine disruptors. This study highlights the adaptability of Huh7 cells in pharmacological and toxicological applications, specifically for investigating the mechanisms of liver disease specific to gender and the effects of hormonemodulating medications on hepatic lipid profiles.

Effective liver-targeted therapy utilising mannose-modified liposomes for targeted gene delivery into Huh7 Cells

This study showed that mannose-modified liposomes can effectively deliver genes into Huh7 cells while improving transfection efficiency and hepatic specificity. The study is essential for creating liver disease treatment strategies that do not include viral gene therapy. The scientists assessed these nanocarriers cellular absorption, reporter gene expression and safety profile using Huh7 cells as a model. The results validate the use of Huh7 cells in nanomedicine, particularly for evaluating RNA-based treatments, gene editing technologies and liver-targeted delivery systems. This demonstrates the value of Huh7 cells in liver-directed pharmacological innovation, formulation screening and delivery mechanism optimisation (Yoshida *et al*., 2013) [27].

Treatment effects of metal complexes against Huh7 Liver Cancer Cells

The cytotoxic and anticancer characteristics of several metal-based complexes tested against Huh7 liver cancer cells are the main topic of this review. The work demonstrates how Huh7 cells is a reliable platform for screening anticancer chemicals, including as complexes of copper, ruthenium and platinum. The authors show that Huh7 cells are very sensitive to the oxidative stress, induction of apoptosis and DNA damage brought on by these substances. According to (Ming *et al*., 2013) [14], this makes Huh7 cells a useful model in onco-pharmacology, particularly for assessing new chemotherapeutics, combination therapies and agents that mitigate drug resistance in hepatocellular carcinoma (HCC).

The anti-cancer effects of thymoquinone, a bioactive compound from *Nigella Sativa*, in Huh7 Hepatocellular Carcinoma Cells

This study assessed the anti-cancer effects of thymoquinone, a bioactive compound from *Nigella sativa*, in Huh7 hepatocellular carcinoma cells. It did this by examining the antiproliferative and pro-apoptotic activities of the compound. There is evidence that thymoquinone reduces proliferation markers, triggers caspase-mediated apoptosis and induces cell cycle arrest in a dose-dependent manner. These findings confirmed that Huh7 cells is a responsive platform for investigating naturally occurring substances that may have chemotherapeutic uses. Huh7 cells is a dependable tool for anti-cancer pharmacology and nutraceutical drug development in the context of liver cancer treatment, as the research confirms its relevance in discovering and characterising apoptosis-inducing compounds and evaluating their molecular pathways (Elkady *et al*., 2014) [5].

Examining autophagy-modulating substances in Huh7 Cells for Steatosis Treatment

The goal of this work was to find potential treatments for hepatic steatosis by assessing autophagy-modulating substances in Huh7 cells under lipid overload. The researchers showed that increasing autophagic flow dramatically reduced intracellular triglyceride buildup using fluorescence microscopy and LC3-II measurement. According to the results, Huh7 cells are very useful for researching lipophagy, which makes them perfect for pharmacological studies that focus on autophagy pathways in MASLD/NAFLD. The study highlights the potential of Huh7 cells in the screening of medications that use autophagy activation to restore lipid homeostasis, a novel and promising treatment approach for fatty liver diseases (Park *et al*., 2016) [16].

Demonstrates the hepatoprotective effects of resveratrol in Huh7 Cells

This study demonstrates the hepatoprotective effects of resveratrol in Huh7 cells exposed to palmitate-induced lipotoxicity by reducing endoplasmic reticulum stress and inflammation. Research has demonstrated that resveratrol suppresses pro-inflammatory cytokines (TNF-α, IL-6) and lowers ER stress markers (CHOP, GRP78). The study shows how Huh7 cells are a useful *in vitro* model for assessing drugs that target inflammation and ER stress, two important pathways in the development of MASLD. Additionally, it bolsters the pharmacological potential of resveratrol as a nutraceutical treatment for liver disorders. The study confirms that Huh7 cells are useful for metabolic screening and anti-inflammatory screening in the study of steatotic liver disease (Lee *et al*., 2020) [12].

Curcumin's protective effect against oxidative stress in Huh7 cells exposed to free fatty acids

This study examined curcumin's antioxidant capacity in Huh7 cells exposed to oxidative stress caused by free fatty acids, simulating MASLD conditions. Curcumin increased the activity of antioxidant enzymes (SOD, catalase), boosted GSH levels and dramatically decreased the production of ROS. The findings supported curcumin's therapeutic application in avoiding oxidative liver injury by confirming its capacity to reduce lipotoxic damage. An efficient platform for simulating hepatic redox imbalance and evaluating antioxidant interventions was the Huh7 cell line. This supports the usefulness of Huh7 cells in liver pathophysiology studies on oxidative stress and nutraceutical screening (Kowalczyk *et al*., 2019) [10].

The AMP-Activated Protein Kinase (AMPK) Pathway on Berberine Significant

Through the activation of the AMP-activated protein kinase (AMPK) pathway, berberine significantly decreased intracellular triglyceride accumulation in Huh7 hepatocytes. This study investigated the lipid-lowering effects of berberine in these cells. The authors demonstrated that berberine increased fatty acid oxidation and down regulated lipogenic genes (SREBP-1c, FAS). Huh7 cells were perfect for examining AMPK-mediated drug actions and hepatic lipid metabolism. In addition to establishing Huh7 cells as a potent screening model for anti-steatotic drugs that target energy metabolism and lipogenesis pathways, our study emphasises the pharmacological potential of berberine in the treatment of MASLD (Kim *et al*., 2018) [9].

The PPARα Pathway, Quercetin has Anti-Steatotic and Anti-Inflammatory Effects in Huh7 Cells

Through the PPARα pathway, quercetin has anti-steatotic and anti-inflammatory effects in Huh7 cells. This study assessed how quercetin, a flavonoid, affected inflammation and fat accumulation in Huh7 cells exposed to free fatty acids. Quercetin activated PPARα, a crucial regulator of lipid metabolism, suppressed pro-inflammatory cytokines and dramatically reduced intracellular triglyceride levels. These results highlight quercetin's potential as a natural treatment for managing MASLD. Huh7 cells validated their use in pharmacological and nutraceutical testing of PPAR-targeting compounds by enabling accurate evaluation of inflammatory markers and lipid regulatory gene expression (Xu *et al*., 2019) [25].

Silymarin Shields Huh7 Cells from Palmitate-Induced Steatosis

By modifying lipid metabolism and oxidative stress, silymarin shields Huh7 cells from palmitate-induced steatosis. This study showed that silymarin, a well-known hepatoprotective flavonoid from *Silybum marianum*, dramatically lowers oxidative stress and lipid accumulation in palmitate-treated Huh7 cells, that MASLD conditions. Silymarin enhanced the activity of antioxidant enzymes, reduced the generation of ROS and altered genes involved in lipid metabolism, including ACC, FAS and CPT1. The results demonstrate its therapeutic potential for hepatic steatosis prevention or treatment. Emphasised the significance of Huh7 cells in pharmacological and nutraceutical research for metabolic liver illnesses by using them as an efficient model for assessing phytochemical therapies and comprehending antioxidant-lipogenic interaction in liver cells.

Pharmacoeconomic Evaluation of Huh7 and common mammalian cell lines in preclinical research

- **HUH7 Cell Line:** The cost-effectiveness, scalability and experimental dependability of the Huh7 cell line for drug screening and toxicological investigations pertaining to the liver constitute its pharmaco-economic feature. Huh7 cells provide a stable, affordable and repeatable substitute for primary human hepatocytes, which are costly, transient and donor-dependent. This makes them appropriate for high-throughput tests. They are very cost-effective for long-term pharmacological and metabolic research due to their ease of culture, availability from repositories (e.g., ATCC, JCRB) and maintained expression of important hepatic genes (Wilkening *et al*., 2003) [24]. Huh7 Cells is perfect for industrial and academic liver pharmacology applications because it lowers operational costs and unpredictability.
- **HEPG2 Cell Line:** Pharmacogenomic studies commonly employ the human hepatocellular carcinoma cell line HepG2 Cells to investigate genetic variants influencing drug metabolism and hepatotoxicity. Despite having lower levels of some cytochrome P450 enzymes than primary hepatocytes, it is still able to express UGTs, GSTs and a number of drug transporters, which makes it appropriate for assessing the impact of polymorphic genes on drug detoxification. HepG2 Cells is very useful for modelling the effects of pharmacogenetic variations on drug-induced liver damage (DILI) and metabolic profile in genetic manipulation experiments using CRISPR or siRNA (Wilkening *et al*., 2003) [24].
- **HEK293 Cell Line:** Derived from human embryonic kidney cells, the HEK293 Cell line is essential for pharmacogenomic research, particularly when examining genetic variants that impact drug response, receptor pharmacodynamics and drug-gene interactions. Polymorphic variants of drug-metabolizing enzymes, ion channels and receptors like CYP450s, ABC transporters and GPCRs can be expressed functionally thanks to its high transfection efficiency. HEK293 cells are crucial for pharmacogenetic biomarker validation and personalised medicine because they are commonly used in CRISPR-Cas9 screens to find genomic determinants of drug resistance and sensitivity (Thomas *et al*., 2005) [21].
- **CHO Cell Line:** Pharmacogenomic studies that examine genetic variations impacting drug response, especially in relation to glycosylation patterns and biopharmaceutical synthesis, frequently employ Chinese Hamster Ovary (CHO) cells. They are perfect for producing recombinant proteins and monoclonal antibodies with specific genetic alterations due to their stable genome and gene editing adaptability. CHO cells facilitate the evaluation of genetic variations in pharmacokinetic-altering genes and glycosylation enzymes, assisting in the creation of tailored, patient-specific treatments. Their use in CRISPR-based genome engineering strengthens their position in functional pharmacogenomics and precision medicine (Kim *et al*., 2012) [8].

- **CACO-2 Cell Line:** In pharmacogenomics, the human colorectal adenocarcinoma-derived Caco-2 cell line is frequently used to investigate intestinal drug absorption, transport and metabolism, particularly with regard to genetic differences in transporters and metabolic enzymes. Caco-2 cells exhibit enterocyte-like characteristics upon differentiation, expressing genes like CYP3A4, P-glycoprotein and SLC transporters all of which are genetically polymorphic and essential for assessing the bioavailability of oral drugs. Caco-2 models support customised drug development and oral formulation optimisation by assessing the effects of genomic variants on drug permeability and efflux (Sun *et al*., 2008) [20].
- **PHH Cell Line:** With their native expression of genetically polymorphic enzymes including CYP450 isoforms, UGTs and transporters like OATP1B1 and BCRP, primary human hepatocytes (PHH) are the gold standard for pharmacogenomic research of hepatic drug metabolism and toxicity. Because PHHs maintain donor-specific genetic backgrounds, it is possible to precisely examine inter-individual heterogeneity in adverse drug responses and therapeutic responsiveness. They are therefore crucial for researching drug-gene interactions, validating pharmacogenomic biomarkers and developing personalised medicine approaches. Their application sheds light on the genotype-phenotype relationships that are essential to clinical pharmacogenetics. (Lauschke *et al*., 2016) [11].

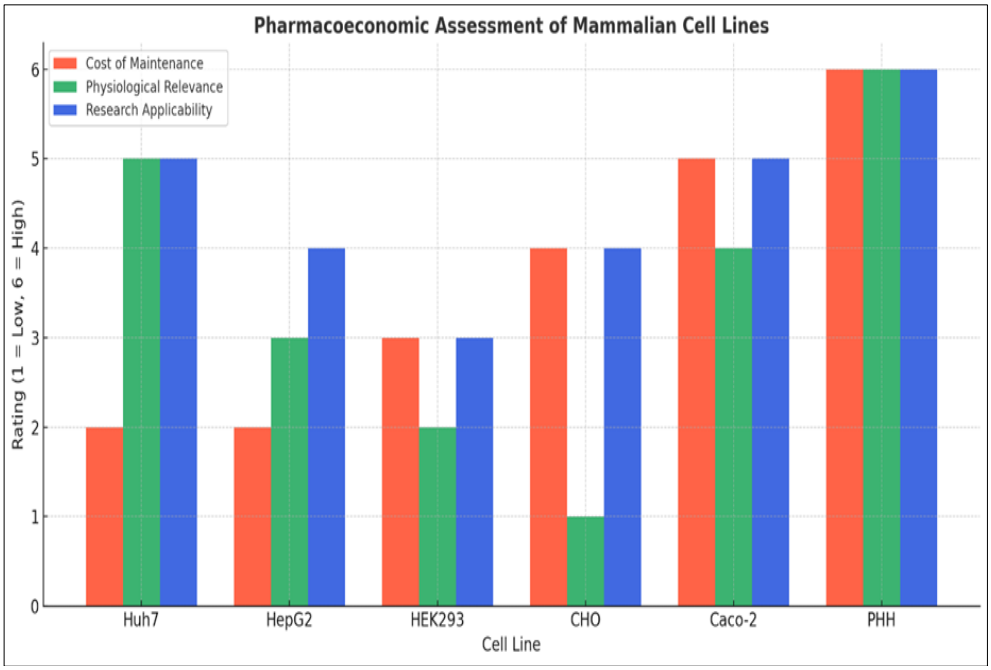

Fig 1: Pharmacoeconomic assessment of mammalian cell lines

Conclusion

In hepatic research, the Huh7 cell line is a crucial tool because it provides a reliable, affordable and repeatable model that closely resembles several hepatocyte functions. Pharmacotoxicology, cancer research, metabolic illness models and virology are just a few of its many applications. Hepatocellular Carcinoma (HCC), drug-induced liver injury (DILI) and Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) have all benefited greatly from the use of Huh7 cells, which have revolutionised the field of hepatitis-C virus (HCV) research. It is possible to precisely evaluate hepatoprotective, antioxidant and anti-steatotic drugs because of their susceptibility to lipid build up, oxidative stress, mitochondrial dysfunction and inflammatory stimuli. Huh7 cells continue to be a viable substitute for primary hepatocytes in spite of their restrictions brought on by their malignant origin, particularly in high-throughput tests and mechanistic investigations. Additionally, the use of genetic engineering in pharmacogenomics and precision medicine has increased due to developments in technologies like as transfection and CRISPR-Cas9. Scalability, long-term viability and experimental reliability are just a few of their pharmacoeconomic benefits that make them a popular option for both academic and commercial research. In conclusion, the Huh7 cell line remains essential for liver-focused pharmacological innovation, contributing significantly to the identification of therapeutic targets, the advancement of our knowledge of liver diseases and the *in vitro* validation of treatment approaches.

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