Bull. Chem. Soc. Ethiop. **2023**, 37(4), 917-929.
DOI: https://dx.doi.org/10.4314/bcse.v37i4.9

ISSN 1011-3924
Printed in Ethiopia
Online ISSN 1726-801X

SYNTHESIS AND CHARACTERIZATION OF QUERCETIN-LAYER DOUBLE HYDROXIDE (LDH) NANOHYBRID AND THEIR ENHANCED ANTIOXIDANT ACTIVITY

Y. Christabel Shaji[1], D. Deena Rose[2], C. Ramesh Kannan[3], M. Aruna[4] and Y. Brucely[3*]

[1]Department of Chemistry, Holy Cross College (Autonomous), Nagercoil-629004, Tamil Nadu, India
[2]Department of Artificial Intelligence, K. Ramakrishnan College of Technology, Tiruchirappalli, Tamil Nadu, India
[3]Department of Mechanical Engineering, SRM TRP Engineering College, Irungalur, Tirchirappali, Tamil Nadu, India
[4]Depatrment of mechanical Engineering, University of Dubai, Academic city, Dubai, UAE

(Received December 13, 2022; Revised February 24, 2023; Accepted February 25, 2023)

ABSTRACT. This research included the synthesis of pristine nitrate-type Zn_2Al-LDH by means of Co-precipitation, which was then followed by hydrothermal treatment. Ion exchange is used to stabilize the produced pristine LDH nano layer, which is used for the encapsulation of bioactive molecules. Quercetin, which has an antioxidant function, is used. XRD was used to investigate the newly synthesized quercetin-LDH (QC-LDH) compound. Quercetin was discovered to be entirely deprotonated as a result of XRD research, and it was also shown to be stabilized in between LDH lattices as a result of electrostatic contact. On the basis of the diphenyl picrylhydrazyl (DPPH) method, the anti-oxidant property was discussed, and it was discovered that the quercetin that was free from the LDH layer helped as an owing antioxidant to scavenge DPPH radicals in ethanol solvent at concentrations ranging from 80-100%, depending on the concentration level. The powder X-ray diffraction patterns indicate that the incorporation of quercetin into the interlayer led to an expansion of the interlayer arrangement to 0.88 and 1.46 nm, respectively. According to the findings of a variety of characterization techniques, the QC-LDH may be regarded as a good antioxidant material with potential drug delivery system.

KEY WORDS: Layer double hydroxide, Antioxidant activity, Quercetin, Biocompatibility

INTRODUCTION

Cancer has increasingly become one of the most significant obstacles to be faced in terms of the world's public health. According to the data published by the World Health Organization (WHO), cancer is responsible for the deaths of 8.97 million individuals worldwide each year. As a result of this, cancer has now surpassed coronary artery disease to become the second leading cause of death, falling just behind ischemic heart disease as the leading cause of death. Due to the fact that tumors are made up of cancer cells that are encircled by normal healthy cells within the extracellular matrix, such as adipocytes and immune cells, tumours can only be removed surgically and the microenvironment of a tumors is both complicated and distinct. In compared to typical rates of cell growth, it is distinguished by an abnormally rapid rate of cell growth, which is one of its defining characteristics. Because it is now common knowledge that the metabolic state and consumption power for nutrients of cancerous cells is significantly higher than that of normal cells and that they are distributed very widely, organisms are weak and are unable to compete with tumors for nutrition. This is because cancerous cells consume nutrients at a much faster rate than normal cells do. This is due to the fact that cancerous cells spread very extensively. In the meanwhile, the endothelium is unable to provide an adequate quantity of nutrients as a

*Corresponding author. E-mail: brucely2k6@gmail.com

result of such fast expansion, and certain cells are unable to proliferate in such an environment since it is empty of fundamental nutrients.ne of the flavonoids with the greatest widespread recognition has been a traditional part of the human diet for a very long time. The consumption of quercetin has been widely linked to a great number of health benefits, such as antioxidant, anti-inflammatory, antiviral, and anticancer properties, in addition to the ability to alleviate the symptoms of certain cardiovascular diseases (such as heart disease, hypertension, and high blood cholesterol) [1-3]. As previous phytochemical studies on ocimumtennuiflorum shown, flavonoids are a crucial bioactive chemical with excellent biological and pharmacological advantages. Flavonoids, a class of polyphenol secondary metabolites, are presented broadly in plants and diets. They are believed to have various bioactive effects including anti-viral, anti-inflammatory, cardioprotective, anti-diabetic, anti-cancer, anti-aging, etc. Their basic structures consist of C_6-C_3-C_6 rings with different substitution patterns to produce a series of subclass compounds, and correlations between chemical structures and bioactivities have been studied before. Natural compounds derived from plant extracts, including flavonoids, alkaloids, polyphenols, and carotenoids, provide a rich ground for the development of cancer therapies that are more effective and have fewer adverse effects. Phytochemicals, which are derived from plant extracts, make for great chemotherapeutic agents due to the fact that they are non-toxic, readily accessible, and economical [4-8]. The pervasive presence of flavonoids in plant life may be attributed to their benzo-pyrone like structural makeup. Flavonoids make up a broad category of polyphenolic chemicals. The phenylpropanoid pathway is responsible for their synthesis. The findings that are available tend to suggest that secondary metabolites of phenolic origin, including flavonoids, are responsible for the wide diversity of actions that are pharmacological [9-10]. Quercetin easily oxidizes under mild conditions and shows sensitivity to pH; these decrease the biological functionality of quercetin. The quercetin is not stable in plasma and needs an encapsulation system to decrease or avoid degradation. Quercetin is a dietary polyphenol that offers a variety of health advantages, including anti-inflammatory, antioxidant, and anti-diabetic characteristics. Quercetin may be found in foods including apples, onions, and tea. However, its use is restricted since it has a poor bioavailability, rapid elimination from the body, and the need of taking very large dosages in order to have any positive benefits. For this reason, it is essentially necessary to use methods that are able to keep the concentration of quercetin in the body blood or targeted tissues at the correct amount for an extended period of time in order to get productive results [11-12]. Especially opposed to free medications, drug-intercalated LDH is more effective at entering the cellular membrane. This allows it to sustain high levels of intracellular drug concentration and, as a result, overcomes the problem of multi-drug confrontation in cancer. The drug delivery system (DDS), also known as the technique of distributing a pharmaceutical substance, is an essential component in order to achieve the desired therapeutic effect. Absorption, drug release profile, distribution, and elimination are some of the qualities of a medicine that may be modified using DDS technology. These modifications can result in increased effectiveness, decreased toxicity, improved patient adherence, and improved appropriateness. During the course of the past several researches, a minimum amount of research and development has been focused on the intercalation of physiologically functionalized molecules into biocompatible two-dimensional inorganics. Two dimensional layered resources, such as layered double hydroxides (LDHs), are known to have a high cellular uptake efficiency, biocompatibility, highly anisotropic structure, physical strength, and chemical inertness. As a result, the intercalation of biofunctional molecules into LDHs has been identified as a way to improve the biological obtainability of 2D layered resources [13-15].

Intercalated anions have the capability of being chemically stabilized by attractive forces as well as being acutely and chronically shielded from the harsh surroundings encountered outside by the metal hydroxide sheets, may be released from the LDH lattice in a regulated way after the conclusion of an anion exchange process. As a result, there has been a lot of research made to interpolate bio-functional molecules into LDHs with the purpose of using them in medical application [16-17]. There have recently been many synthetic routes to organic-LDH nanohybrids.

These routes include co-precipitation, successive hydrothermal treatment, restoration, and ion exchange. On the other hand, some hydrophobic organic guests that are stereo chemically complicated have proved to be challenging to intercalate into the LDH lattice. The quercetin anions were unable to enter the interlayer gaps of LDHs through co-precipitation or ion exchange, no matter how they were synthesized, as suggested by the conventional ion exchange and co-precipitation routes. This was most likely due to the kinetic significant barrier in the charge transfer reaction [18-22]. Crystallographic structure determination has typically been accomplished by the use of X-ray diffraction (XRD) as a method for investigating the structure of crystalline materials. Following the treatment of the crystal with a collimated X-ray beam, measurements were taken to determine the angles at which the beam was diffracted. Crystals are able to diffract light with a wavelength that falls within the range of interatomic separations, which at the time fell within the range of 2–3 atomic separations. This is because crystals include properties that occur in a pattern that is repeated over and over again [23].

An alternate method of generating Ni-Cr-LDH nanohybrids intercalated with OD polyoxotung state layer by layer nanohybrids, ZnAl-LDH/PMo12 nano-hybrids has been presented, and it involves the use of an exfoliation and reassembling process [24-26]. To better understand quercetin's chemical stability and regulated release from its host LDH, researchers in the present work created a chemically and structurally well-defined quercetin-LDH nanohybrid, quercetin demonstrates a radical scavenging activity of 96%, 2-diphenyl-1-picrylhydrazyl, and it also proves a high level of radical scavenging activity at low temperatures in comparison to its activity at atmospheric temperature, whereas QC-LDH confirmations only 80% repressive effect at concentration of 20 µg/mL.

EXPERIMENTAL

Materials

Zinc nitrate hexahydrate $Zn(NO_3)_2 \cdot 6H_2O$, aluminum nitrate nonahydrate $[Al(NO_3)_3 \cdot 9H_2O]$, sodium hydroxide (NaOH) and water were used for the preparation of pristine and QC-LDH preparation. Sodium hydroxide (NaOH), ethanol and quercetin were purchased from E-Merk, India. In every experiment, only decarbonated water was used. Figure 1 shows the molecular structure of zinc nitrate hexahydrate.

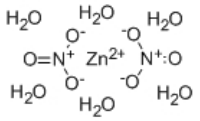


Figure 1. Molecular structure zinc nitrate hexahydrate.

Preparation of Zn2Al-NO3/LDH pristine

The synthesis of pure pristine LDH included a procedure that started with direct co-precipitation and proceeded with heat method at 100-120 ºC. In a setting that included nitrogen, an aqueous solution of zinc nitrate (0.012 M) and aluminum nitrate (0.006 M) was titrated with a solution of sodium hydroxide (0.5 M), and the results were read as the concentration of nitrogen in the solution. After the tunings, the pH of the solutions was brought down to a range of 7.5-8. The precipitate that was produced as a consequence was aged for one hour before being recovered by centrifugation. Following that, it was washed five times with water that had been decarbonated, and then it was dried at a temperature of 120 ºC for a period of six hours. Figure 2 represents the schematic setup for Co-precipitation setup.

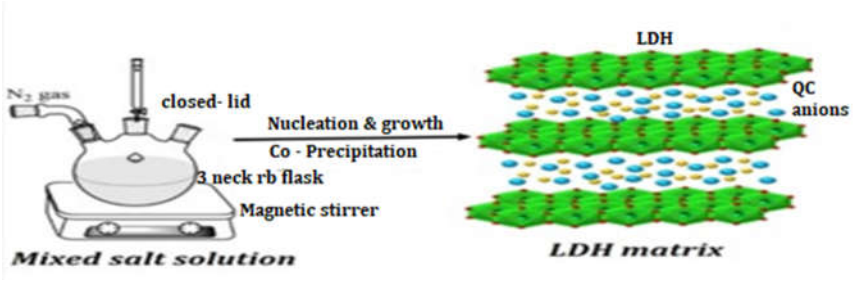


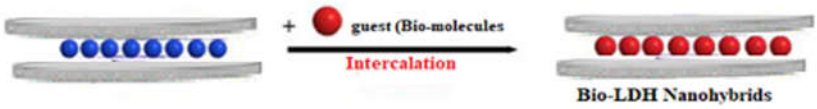
Figure 2. Schematic representation of co-precipitation method.

Exfoliation-reassembly route to QC-LDH nanohybrid

The white precipitate that had been hydrothermally treated was initially dispersed in formamide at a concentration of 1 g/100 mL and mechanically agitated for 48 hours prior to the exfoliation and reassembly procedure. The pure LDH is another name for this precipitate. Methods of centrifugation can be split into the following three categories: 1) sedimentation-based separation or centrifugation (SBS), which separates nanosheets based on the differences in their masses; 2) sedimentation-based density gradient ultracentrifugation (sDGU), which also separates nanosheets based on their masses, but with more precise lateral size separation via controlled density gradient; and 3) isopycnic density gradient ultracentrifugation (iDGU), which separates nanosheets based on the differences in their buoyant density [27]. In order to separate the exfoliated and suspended nanosheets, the colloidal solution was centrifuged at 2000 rpm for 5 min. To complete the procedure, these nanosheets were employed. LDH nanosheets were dissolved in an aqueous solution with the specified concentrations of 1.0, 1.5 and 2.0 times the anionic exchange capacity (AEC) of pristine LDH, respectively. This was done in order to examine the impact of the three concentrations on the QC's performance characteristics. Each of the following steps was carried out individually. Additionally, all reassembly procedures had to be maintained for 3 hours at a temperature of 4 ^{o}C to stop the breakdown of QC under natural settings (seasonal fluctuations in climatic and atmospheric conditions) from unexfoliated precipitates. A mixture of decarbonated water and ethanol in the ratio of 1:1 in solution was used to wash the QC-LDH nanohybrid five times before it was finally freeze-dried to remove the nitrate ions that had been attached to it and the QC ions that had not associated with it.

Ion echange method for synthesis of QC-LDH nanohybrid

Ion exchange is a technique of water treatment in which one or more unwanted ionic pollutants are eliminated from water by exchanging them for another ionic component that is either not unpleasant or is problematic to a lesser degree. In this study, Zn/Al LDH-Quercetin was synthesized using an ion-exchange technique. In the first step of the process, 1.06 g of quercetin were titrated with a 1 mL solution of sodium hydroxide (NaOH). This solution was then added to 50 mL of an aqueous interruption that contained 1.0 g of Zn/Al LDH precursor. This combination was agitated very vigorously for twenty-four hours at room temperature in an atmosphere of nitrogen. After that, the goods were given five separate washings in a solution consisting of decarbonated water and ethanol at a ratio of 1:1, and then they were dried [28-29]. Figure 3 (a) and (b) shows the representation intercalation routes to layered nanohybrids of ion-exchange method and setup.



(a)

(b)

Figure 3. (a) Intercalation routes to layered nanohybrids of ion -exchange and (b) ion-exchange method setup.

Synthesis of QC-LDH nanohybrid through Co-precipitation method

Figure 4 represents a diagrammatic illustration of the hybrid material Zn/Al LDH-Quercetin co-precipitation technique. It was processed by gently adding quercetin aqueous solution (50/50 v/v) into a combination of molar $Zn(NO_3)_2 \cdot 6H_2O$ and $Al(NO_3)_3 \cdot 9H_2O$ aqueous solutions while it was being exposed to an environment of nitrogen. The ratio of zinc to aluminium was set at 2. Through the simultaneous addition of 1 M of NaOH, we are able to keep the pH stable within the range of 7.5-8.0. After that, the slurry is churned for a full twenty-four hours at room temperature. The resulting items underwent a meticulous process in which they were cleaned five times with a solution that had equal parts decarbonated water and ethanol before being dried.

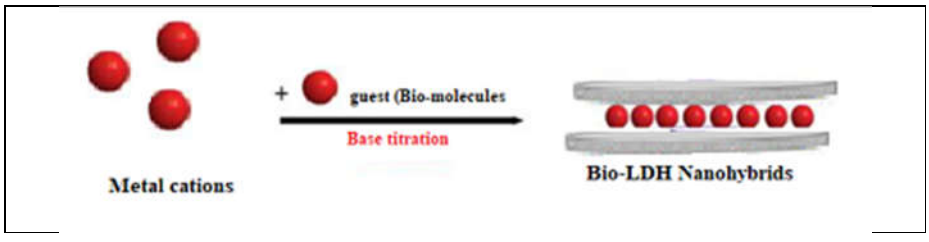


Figure 4. Intercalation routes to layered nanohybrids co-precipitation.

Characterization of QC-LDH nanohybrids

Powder X-ray diffractometer (SHIMADZU FT-IR Affinity-1 spectrophotometer) with Nifiltered Cu-Ka radiation (l = 1.5418) was used to acquire (00l) diffraction peaks, which were then used for structural studies of both QC-LDHs and the pure LDH. The diffractometer was done at 40 kV voltage and 30 mV current. In order to perform an analysis using the Fourier transfer infrared (FT-IR) spectroscopic technique, the samples were prepared using the conventional KBr disc procedure. The results were then examined using a JASCO FT-IR 6100 spectrometer in the range 400–4000 cm^{-1}. The image was taken by tapping mode on a Veeco Dimension 3100 scanning force microscope, which was used to perform atomic force microscopy.

Antioxidant activity test of QC-LDH

The DPPH free radical scavenging activity is used to evaluate the antioxidant properties of quercetin and hybrids containing quercetin and LDH. Using the stock solution as a starting point, researchers can generate solutions with lower concentrations of quercetin and quercetin-LDH (0.5-20 µg/mL) in ethanol and PBS: 4 ºC as solvents, respectively. These solutions were prepared by serially diluting the stock solution. The 0.1 M solution of DPPH in ethanol that has just been made is fresh. To the ethanol solution of DPPH, samples of varying concentrations were added in increments of a volume equal to 2 mL. Each of the tests was carried out in a dark environment at room temperature for the duration of 30 min, and the absorbance was measured at a wavelength of 517 nm. The observation of a decreased absorbance is characteristic of the increased DPPH scavenging activity that is present.

Photo-stability test of QC-LDH

The UV light stability test is carried out with both pure quercetin and quercetin-LDH nanohybrid in order to determine the photosensitivity of quercetin-LDH nanohybrid. In a glass container that is placed in the presence of light, the needed quantity of samples is weighed and investigated. The UV-Visible Spectrophotometer (HITACHI U-2900) was used to measure the amount of exposure to UV radiation as well as its effects.

RESULTS AND DISCUSSION

Powder X-ray diffraction analysis

The nanolayered structure of Zn/Al-LDH is outfitted in order to serve as a host for quercetin. Figure 5 (a), (b), (c) and (d) shows the XRD pattern of quercetin and LDH, the layered double hydroxide structure is illustrated by exhibiting the basal peaks of planes hkl (003), (006), and (009). By observing the values that correspond to consecutive diffractions using basal planes, one can see that the values generally coincide with one another, as shown by the equation d(003) = 2d(006) = 3d(009) for Zn/Al-LDH. It reveals the tightly packed stacks of brucite-like layers that are organized along the axis c. It has been shown via the ion exchange pathway (QC-LDH-I) that the creation of material with a well-organized nanostructure is not complete at the ~2AEC stage of quercetin. Since the fundamental configuration of QC-LDH-I is 8.9Å, the nitrate anions cannot be substituted in any way. For the purpose of the Co-Precipitation approach (QC-LDH-Co), the metal salts might on occasion be thermodynamically unstable [23]. The synthesis of QC is more challenging than that of LDH because of the stereo-chemical complexity, size, and charges of QC under the pH condition of synthesis, as well as the difference in the hydrophilic and hydrophobic natures of QC and LDH lattice [19, 20], it is quite clear that intercalating quercetin into Zn-Al-layered double hydroxide by Ion-exchange method one could be considered as an ideal route to QC-LDH nanohybrid.

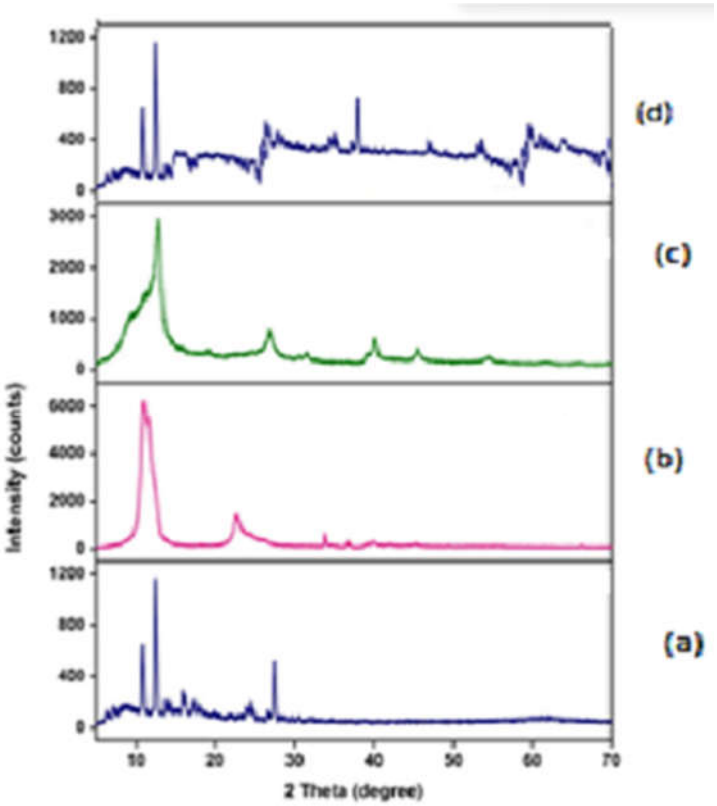


Figure 5. (a) XRD patterns of quercetin, (b) XRD patterns of LDH, (c) XRD patterns of QC-LDHby ion-exchange method and (d) XRD patterns of QC-LDH by co-precipitation method.

FT-IR analysis of QC-LDH nanohybrid

FT-IR spectra are analyzed in order to provide evidence that quercetin may be intercalated into layered double hydroxide interlayers. The intercalation of quercetin into the interlayer arrangement of Zn-Al layered double hydroxide is present in all nanohybrids, as can be shown in Figure 6. The binding of the cellular fragment into the LDH surface or the realization of intercalates is known to give rise to an increase in the fluctuations in the IR spectra of the interacting species. A broad absorption band may be seen in the region of 3000-3500 cm^{-1}. This band is caused by the formation of O-H stretching in the hydroxyl group of LDH as well as substantially adsorbed water molecules. The presence of a prominent band at 1384 cm^{-1} may be attributed to the nitrate group's characteristic v3. The bending vibration of the v(O-H) bond causes the absorption band at 1630 cm^{-1}. The presence of C=O stretching vibrations in a carboxylic group can be deduced from the observation of two bands at 1705 cm^{-1}. Additionally, the presence of a band at 1620 cm^{-1} indicates that C=C stretching vibrations are present, and a band that can be found at 1542 $cm^{-1}$is due to COO asymmetric stretching. On the other hand, quercetin-LDH shows the majority of the vibration related with both and Zn Al-LDH, while a number of additional vibrations are intersecting with each other.

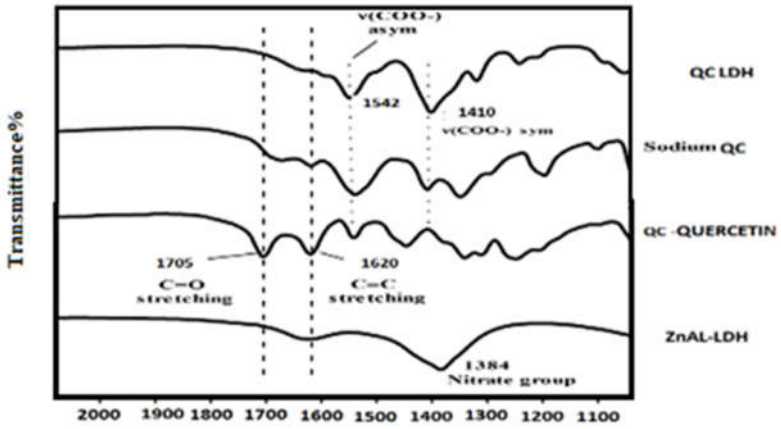


Figure 6. Fourier transform infrared spectra of (a) Zn_2AlLDH, (b) quercetin, (c) sodium gallate and (d) QC-LDH.

The COO asymmetric stretching and the COO symmetric stretching both contribute to the appearance of a new band at 1542 and 1410 cm^{-1}, respectively. In addition, the lack of a band located at 1381 cm^{-1} in the spectra of ZnAl-LDH-quercetin provides further evidence that the interlayer nitrate anions are present. According to the findings of this FT-IR spectrum study, quercetin has undergone full deprotonation to become quercetin anion and is held in place in between LDH lattices by means of electrostatic contact [24-27].

UV spectral studies

Throughout many cases, the assessment of the data those other kinds of structural studies have provided may benefit greatly from the use of UV-visible spectra. Ethanol was used to dissolve the quercetin and quercetin-LDH nanohybrid that had been generated by the ion exchange process. The electronic spectra of these two compounds were then recorded in the region of 200-800 nm [30-32]. As a result of intercalation, quercetin exhibits an absorption band at 380 nm, while quercetin-LDH nanohybrids absorb light at 258 nm. During intercalation, the band moves downward to a lower position [33]. This difference is because quercetin is able to penetrate the surface of LDH platelets and get absorbed therein. Figure 7 shows the UV absorbance of quercetin and quercetin-LDH.

Antioxidant assay

Quercetin has a number of beneficial properties, one of which is its powerful antioxidant activity. It is critical to conduct an analysis upon intercalation in the matrix to determine whether or not the quercetin molecules have maintained their chemical integrity in terms of their antioxidant activity. In the anti-oxidant experiment, the free-radical scavenging activity of DPPH radicals led the way, followed by the quercetin and quercetin-LDH hybrid. The ability of quercetin-LDH to scavenge DPPH radicals is compared with the capacity of quercetin, which serves as a reference. We test two different solvents, ethanol and PBS, at the temperature necessary, which is described further down. An absorption at 517 nm in the clear range with a dark purple hue may be seen when the DPPH solution is newly produced. UV studies demonstrate that the absorption maxima at 517 nm vanish when quercetin and quercetin-LDH are disseminated in DPPH solution for thirty

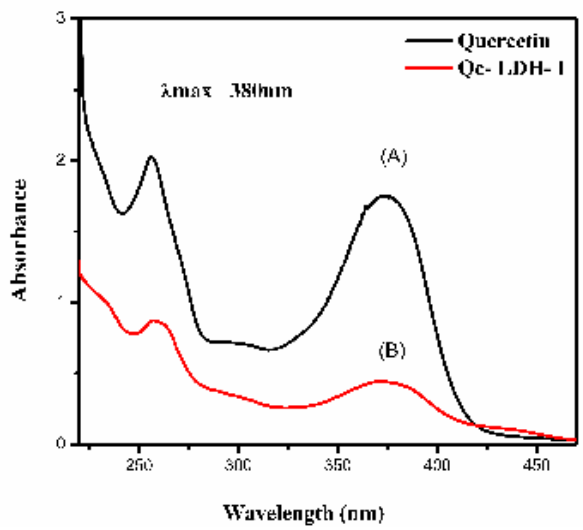


Figure 7. UV-visible spectra of QC & QC -LDH-I.

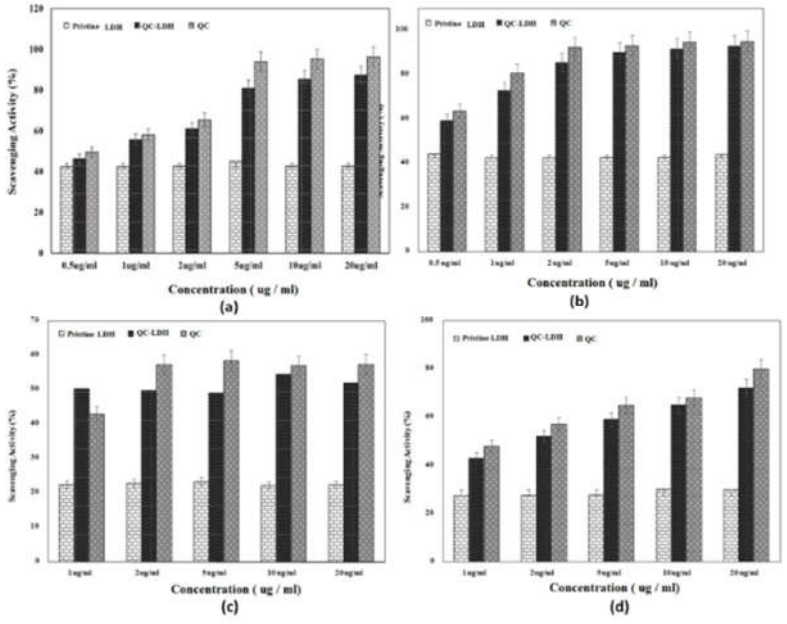


Figure 8. (a) concentrations of Pristine LDH, QC & QC- LDH radicals by spectrophotometry @ Ethanol Solvent in Room Temp (b)) concentrations of Pristine LDH, QC & QC- LDH radicals by spectrophotometry @ Ethanol Solvent in Ethanol Solvent with 4 °C, (c)) concentrations of Pristine LDH, QC & QC- LDH radicals by spectrophotometry @ PBS Solvent in Room Temp (d) concentrations of Pristine LDH, QC & QC- LDH radicals by spectrophotometry @ PBS Solvent in Ethanol with 4 °C.

minutes at room temperature in a dark box. In both cases, the solutions fade to light yellow. The UV tests reveal that the absorption maxima at 517 nm diminish when quercetin and quercetin-LDH are distributed in DPPH solution for 30 minutes at room temperature. Both solutions eventually become a pale yellow colour. According to the findings, quercetin exhibits 96% DPPH radical scavenging activity in ethanol at 37 °C as a solvent, and it also exhibits significant scavenging activity at low temperatures compared to room temperature, but quercetin-LDH exhibits only 80% inhibitory impact at a dosage of 20 µg/mL. Antioxidant action seems to be "concentration-dependent," according to this study. According to Figure 8(d), the antioxidant activity increases in a concentration-dependent manner when PBS 4 °C is employed as the solvent. As a PBS solvent at room temperature, however, its breakdown occurred. quercetin-LDH has a lower DPPH radical activity than quercetin at lower concentrations. It's because DPPH radicals need a little more time to spread across the interlayer's. Antioxidant properties are thus dependent on the quantity of quercetin that is distributed from the hybrids. Due to a significant electrostatic contact between intercalated quercetin and LDHs, the quercetin from 15 quercetin-hybrids partially diffused. Generally speaking, quercetin-capacity LDH's to scavenge radicals is comparable to that of quercetin. The explanation for this is because the intercalation of quercetin anions into the interlayer area has no effect on the hydrogen-atom donating capacity or antioxidant activity.

Photo stability test of quercetin-LDH nanohybrid

It can be seen in Figure 9 (a) and (b) that UV-Vis spectra of quercetin and quercetin-LDH solutions that were not exposed and those that have been exposed are exhibited, correspondingly. Because of the carboxylic acid group's connection to the benzene ring and the hydroxyl groups in the *meta*- and *ortho-para*-positions of the ring, quercetin solutions exhibit two absorbance maxima at 382 and 260 nm, respectively. Due to the rise in irradiation, the peak overall maximum absorbance decreases. Thus, irradiation effectively breaks down quercetin.

The peak at 274 nm becomes smaller as time goes on, relative to the peak at 0 min. Light-stable quercetin-LDH nanohybrids have been a success for us. As a result of the dispersion of drug molecules at a molecular level, stability of the drug is only relevant in nanohybrid systems because of the greater likelihood of interaction. UV light is used to determine the constancy of quercetin. The quercetin-LDH nanohybrid and the pure quercetin are both UV-resistant. UV radiation reduces the quercetin concentration of pure quercetin and quercetin-LDH nanohybrid by about 72% after just 0 to 120 min of exposure. When exposed to UV radiation, quercetin-LDH nanohybrids remain more stable. When compared to pure quercetin before intercalation, the intercalated form's light constancy is greatly improved. This quercetin-LDH nanohybrid might be used as a new medication storage mechanism, according to the findings.

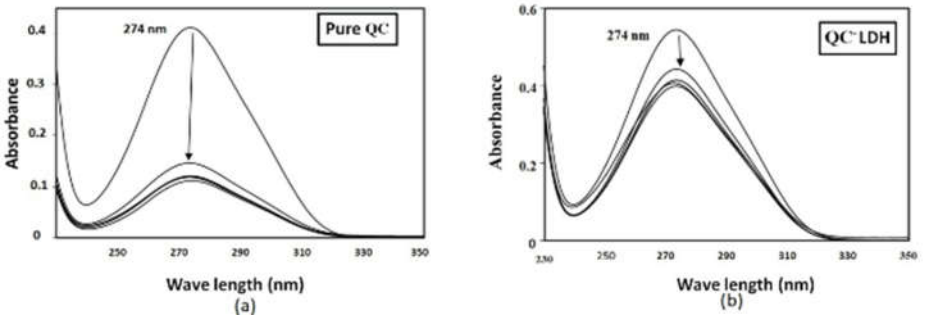


Figure 9. (a) UV-Visible absorption spectra of photosensitized decomposition of quercetin and (b)QC–LDH.

CONCLUSIONS

Nanohybrids of the Pristine-LDH and Quercetin-LDH types were created for the purpose of this research by intercalating Quercetin into Zn-Al-layered double hydroxide using the ion-exchange technique and co precipitation method. The powder X-ray diffraction patterns revealed that the incorporation of quercetin anion into the interlayer is responsible for the growth of the interlayer arrangement to 0.89 and 1.15 nm, respectively. The FT-IR spectra showed that quercetin had been completely deprotonated into quercetin anion and that it was being kept in place in between LDH lattices by electrostatic contact. The QC molecules were released from the QC-LDH nanohybrid in a controlled manner at a temperature of 4 ºC and a pH of 7.4 based on the behavior of quercetin when it is released from the LDH lattice. It was also proven that the QC-LDH nanohybrid may be an effective antioxidant that could scavenge DPPH radicals with an activity of 93 percent or higher in ethanol for QCLDH, depending on the concentration level.

REFERENCES

1. Mattiuzzi, C.; Lippi, G. Current cancer epidemiology. *J. Epidemiol. Glob. Health* **2019**, 9, 217-222.
2. Hinshaw, D.C.; Shevde, A. The tumor microenvironment innately modulates cancer progression. *Cancer Res*. **2019**, 79, 4557-4566.
3. Gonzalez-Valdivieso, J.; Girotti, A.; Schneider, J.; Arias, F.J. Advanced nanomedicine and cancer: Challenges and opportunities in clinical translation. *Int. J. Pharm.* **2021**, 599, 120438.
4. Rishi, K.M.; Anju, M. Principles of pharmacology in the eye. *World. J. Pharm. Res.* **2013**, 2, 1544-1550.
5. Mohammad-Taghi, M.; Ali, K.; Somayeh, A. Anti-adenovirus activity, antioxidant potential, and phenolic content of dried flower buds of Syzygium aromaticum extract in HEp2 cell line. *Chin J. Nat. Med.* **2016**, 14 196-202.
6. Karna, P.; Gundala, S.R.; Gupta, M.V.; Aneja, R. Polyphenol-rich sweet potato greens extract inhibits proliferation and induces apoptosis in prostate cancer cells in vitro and in vivo. Carcinogenesis **2011**, 32, 1872-1880.
7. Naiemeh, M.; Mir, S.S. Application of whey protein-alginate particles coated by black seed oil as a biocompatible carrier of quercetin at treating non-alcoholic fatty liver disease. *J. Functional Food.* **2021**, 86, 104728.
8. Wang, T.Y.; Li, Q.; Bi, K.S. Bioactive flavonoids in medicinal plants: Structure, activity biological fate. *Asian J. Pharm. Sci.* **2018**, 13, 12-23.
9. Mahomoodally, M.F.; Gurib-Fakim, A.; Subratty, A.H. Antimicrobial activities and phytochemical profiles of endemic medicinal plants of Mauritius. *Pharm. Biol.* **2005**, 43, 237-242.
10. Pandey, K. Anti-staphylococcal activity of a pan-tropical aggressive and obnoxious weed Pariheniumhisterophorus: an in vitro study. *Natl. Acad. Sci. Lett.* **2007**, 30, 383–386.
11. Sudipta, S.; Arun, K.M.; Sunil, K. Controlled drug delivery vehicles for cancer treatment and their performance. *Signal Transduct Target Ther.* **2018**, 3, 7-12.
12. Del, A.M.; Gutiérrez, S.; Martín, C.; Rives, V.; Rocha, J. Synthesis and characterization of layered double hydroxides (LDH) intercalated with non-steroidal anti-inflammatory drugs (NSAID). *J. Solid State Chem.* **2004**, 177, 3954-3962.
13. Rives, V.; Arco, M.; Martín, C. Intercalation of drugs in layered double hydroxides and their controlled release: A review. *Appl. Clay Sci.* **2014**, 88-89, 239-269.
14. Choy, J.H.; Kwak, S.H.; Jeong, Y.J.; Park, J.S. Inorganic layered double hydroxides as nonviral vectors. *Anrew. Chem. Int.* **2000**, 39, 4041-4045.
15. Choi, S.J.; Choi, G.E.; Choy, J.H. Anticancer drug encapsulated in inorganic lattice can overcome drug resistance. *J. Mater. Chem.* **2010**, 42, 9463-9469.

16. Choi, G.; Piao, H.; Kim, M.H.; Choy, J.H. Enabling nanohybrid drug discovery through the soft chemistry telescope. *Ind. Eng. Chem. Res.* 2016, 55, 11211-11224.
17. Kong, X.; Jin, L.; Wei, M.; Duan, X. Antioxidant drugs intercalated into layered double hydroxide: structure and in vitro release. *Appl. Clay Sci.* **2010**, 49, 324-329.
18. Arratia-Quijada, J.; Fuentes, R.; Saavedra, K.J.P. Layered double hydroxide as a vehicle to increase toxicity of gallate ions against adenocarcinoma cells. *Molecule* **2016**, 21, 928-936.
19. Liu, Z.; Ma, R.; Osada, M.; Iyi, N.; Ebina, Y. Synthesisanion exchange and delamination of Co-Al layered double hydroxide: assembly of the exfoliated nanosheet/polyanion composite films and magneto-optical studies. *J. Am. Chem. Soc.* **2006**, 128, 4872-4880.
20. Kong, X.; Jin, L.; Wei, M.; Duan, X. Antioxidant drugs intercalated into layered double hydroxide: structure and in vitro release. *Appl. Clay Sci.* **2010**, 49, 324-329.
21. Brucely, Y.; Christabel, K.; Krishnaraj, R. Synthesis and characterization of natural fibre with ZnO nanocomposites. *Int. J. Interact. Des. Manuf.* **2022**, 45, 88-94.
22. Xu, Y.; Huang, W.; Chen, X.; Ge, F.; Zhu, R.; Sun, L. Self-assembled ZnAl-LDH/PMo12 nano-hybrids as effective catalysts on the degradation of methyl orange under room temperature and ambient pressure. *Appl. Catal. A: Gen.* **2018**, 550, 206-213.
23. Padalkar, N.S.; Sadavar, S.V.; Shinde, R.B.; Patil, A.S.; Patil, U.M.; Dhawale, D.S.; Bulakhe, R.N.; Kim, H.; Im, H.; Vinu, A.; Lokhande, C.D.; Gunjakar, J.L. Layer-by-layer nanohybrids of Ni-Cr-LDH intercalated with 0D polyoxotungstate for highly efficient hybrid supercapacitor. J**.** Colloid Interface Sci**. 2022,** 616, 548-559**.**
24. Viscusi, G.; Bugatti, V.; Vittoria, V.; Gorrasi, G. Antimicrobial sorbate anchored to layered double hydroxide (LDH) nano-carrier employed as active coating on Polypropylene (PP) packaging: Application to bread stored at ambient temperature. *Future Foods* **2021**, 4, 100063.
25. Bonaccorso, F.; Bartolotta, A.; Coleman, J.N.; Backes, C. 2D-Crystal-based functional inks. *Adv. Mater.* **2016**, 28, 6136
26. Birjees, B.; Shahabuddin, M.; Mahroof, T.; Bhanger, M.I. Synthesis, characterization and antioxidant activity copper–quercetin complex. *Spectrochim. Acta* **2009**, 71, 1901-1906.
27. Ghotbi, M.Y.; Hussein, M.Z. Gallate–Zn–Al-layered double hydroxide as an intercalated compound with new controlled release formulation of anticarcinogenic agent. *Phys. Chem. Solids*. **2010**, 71, 1565-1570.
28. Shafiei, S.S.; Solati-Hashjin, M.; Asadi-Eydivand, M.; Osman, N.A. Epigallocatechin gallate/layered double hydroxide nanohybrids: preparation, characterization, and in vitro anti-tumor study. *PloS One* **2015**, 10, 0136530.
29. Hirun, N.; Dokmaisrijan, S.; Tantishaiyakul, V. Experimental FTIR and theoretical studies of gallic acid–acetonitrile clusters. *Spectrochim. Acta A* **2012**, 86, 93-100.
30. Hafez, I.H.; Berber, M.R.; Minagawa, K.; Tanaka, M. Design of a multifunctional nanohybrid system of the phytohormone gibberellic acid using an inorganic layered double-hydroxide material. *J. Agric. Food Chem.* **2010**, 58, 10118-10123.
31. Dong, L.; Gou, G.; Jiao, L. Characterization of a dextran–coated layered double hydroxide acetylsalicylic acid delivery system and its pharmacokinetics in rabbit. *Acta Pharm. Sin. B* **2013**, 3, 400-407.
32. Zhang, Y.; Xu, H.; Lu, S. Preparation and application of layered double hydroxide nanosheets. *RSC Adv.* **2021**, 11, 24254-24281.
33. Benitez, F.J.; Real, F.J.; Acero, J.L.; Leal, A.I.; Garcia, C. Gallic acid degradation in aqueous solutions by UV/H_2O_2 treatment, Fenton's reagent and the photo-fenton system. *J. Hazard. Mater*. **2005**, 126, 31-39.
34. Badhani, B.; Sharma, N.; Kakkar, R. Gallic acid: A versatile antioxidant with promising therapeutic and industrial applications. *RSC Adv*. **2015**, 5, 27540-27557.
35. Melo, R.P.; Leal, J.P.; Botelho, M.L. Radiolytic degradation mechanism of gallic acid and its end-products. *Rapid Commun. Mass Spectrum.* **2011**, 25, 218-222.

36. Golonka, I.; Wilk, S.; Musiał, W. The influence of UV radiation on the degradation of pharmaceutical formulations containing quercetin. *Molecules* **2020**, 25, 488-501.
37. He, Y.; He, Z.; He, F.; Wan, H. Determination of quercetin, plumbagin and total flavonoids in *Drosera peltata* Smith Var. Glabrata Y.Z. Ruan. *Pharmacogn. Mag.* **2012**, 8, 263-267.