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Spectroscopic, Visual Test Techniques and Optical Sensors for Determination of Hydrazine and Its Derivatives

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Hydrazine and its analogues are widely used in agriculture and industry for the manufacture of metal films, photographic chemicals, antioxidants, preservatives, insecticides and blowing agents for plastics. It is also found in tobacco. It is used as a scavenger to remove traces of oxygen in boiler feed water system, as antioxidant in nuclear reactor, in military fuel cells and in electrical power plants. Hydrazine and its methyl substituted analogues and unsymmetrical dimethylhydrazine are commonly used as hypergolic propellants in space vehicles, intercontinental ballistic and in other military applications. In addition, hydrazine and its derivatives are considered to be carcinogens. Even low concentration of these substances results in toxic effects in humans. Therefore, there is a strong need in sensors for monitoring of hydrazines to ensure that they are below hazardous levels in order to minimize the risk of exposure.

In this paper a brief review of recent spectrophotometric techniques and optical sensors for the determination of hydrazine and its analogues is presented. Kinetic and flow methods are discussed and compared as a part of spectrophotometric method. The review of optical sensors is divided into subsections based on application of nanoparticles, colorimetric and fluorescent sensors. The techniques of synthesis of new fluorescent reagents, their application for hydrazine detection by visual test method are described and compared. Indicator reactions and main techniques for the visual testing are described. This review comprises the results obtained after 2009.

Keywords: hydrazine, determination, spectrophotometry, fluorescence, sensors

1. Introduction

Hydrazine and its analogues are widely used in agriculture and industry for the manufacture of metal films, photographic chemicals, antioxidants, preservatives, insecticides and blowing agents for plastics. It is also found in tobacco. It is used as a scavenger to remove traces of oxygen in boiler feed water system, as antioxidant in nuclear reactor, in military fuel cells and in electrical power plants [1-5].

Hydrazine and its methyl substituted analogues (monomethyl hydrazine (MMH) and unsymmetrical dimethylhydrazine (UDMH)) are commonly used as hypergolic propellants in space vehicles, intercontinental ballistic and cruise missiles (ICBM), F-16 aircrafts, submarines and in other military and civilian applications [1, 6-9].

In addition, hydrazine and its derivatives are considered to be carcinogens. According to their mutagenic nature, they have impacts on brain and liver resulting in DNA damage. Due to their volatility and highly toxic nature adverse health effects such as skin sensitization, eye irritation, thyroid amyloidosis, respiratory tract problems as well as systemic poisoning were observed at people working with hydrazines. Even low concentration of these substances results in toxic effects in humans [10-15].

In Russian Federation the hygienic standards for the most dangerous ecotoxicants from the considered groups - hydrazine and UDMH - are following: threshold concentration in the air of working area is 0.1 mg/m^3, in atmospheric air - 0.001 mg/m^3, in water for household (fishery) use 0.01 (0.0003) and 0.02 (0.0005) mg/L for hydrazine and UDMH, respectively. Sanitary and hygienic standards for the allowed concentration of UDMH in soils were established at the level of 0.1 mg/kg [16]. The U.S. EPA has not established a reference concentration or dose for hydrazine but it is on the Contaminant Candidate List. The maximum amount of hydrazine in water was proposed to be 0.1 μg/L, in soil 2 μg/kg. Hydrazine is a suspected carcinogen and a threshold limit value in the atmosphere of 1.0 mg/L has been set by OSHA [17].

Detection and determination of hydrazines at threshold limit value (TLV) levels became a significant task in order to avoid negative effects of these compounds. Therefore, effective sensitive methods for detection and determination of hydrazine should be developed.

There is a strong need in sensors for monitoring of hydrazines to ensure that they are below hazardous levels in order to minimize the risk of exposure.

Therefore, determination and monitoring of hydrazine and its derivatives based on molecular absorption and emission methods are discussed in this review. Indicator reactions and main techniques for the determination and visual testing are described and compared. This review comprises the results obtained after 2009.

2. Spectrophotometry

Spectrophotometry is widely used for the determination of hydrazine and its derivatives. Recently, field test systems with visual test techniques gained in popularity. Therefore, in last years around 70 spectrophotometric methods were elaborated.

The methods of indirect determination are based on their strong reducing properties. The involved reagents-oxidizers are characterized by high molar absorption coefficients of the reduced form. For example, the authors in [18] propose spectrophotometric procedure for determination of ppm concentrations of hydrazine which is based on the reaction with potassium permanganate and on the measurement of permanganate discoloring. The absorbance of non-reduced permanganate is measured by the color difference at different wavelengths 546 and 526 nm. Hydrazine can be determined in the range of 100-700 ppm with correlation coefficient of 0.999 and relative standard deviation 1%. The method is successfully applied for the determination of hydrazine in water streams in nuclear reactors/purex process/ boiler water and in polluted water samples.

The reactions of hydrazine synthesis are widely used for the appending of chromophore groups into hydrazine molecules. One of the most widely used reagents for the determination of hydrazine is p-dimethylaminobenzaldehyde (pDMAB). Addition of pDMAB in ethyl alcohol and hydrochloric acid to hydrazine in Atazanavir drug resulted in enhancing of absorbance intensity at $\lambda = 458$ nm. The developed method exhibited linearity range from 0.2 to 2.7 μg/g. The precision is exemplified by relative standard deviation of 0.959% and 0.947%. Percentage mean recovery was found to be in the range of 97-101%, during accuracy studies. The limit of detection (LOD) and limit of quantification (LOQ) were found to be 0.2 μg/g and 0.6 μg/g, respectively [19].

Spectrophotometric methods are compared in the Table 1.

Table 1. Comparison of spectrophotometric methods for determination of hydrazine and its derivatives.

Method	Analytes	Reagent	Object	Analytical range, (ppm)	Ref.
Equilibrium	Hydrazine	Potassium permanganate	water streams in nuclear reactors/ purex process/boiler water, polluted water samples	100 - 700	[18]
	Hydrazine	p-dimethylamino-benzaldehyde (pDMAB)	Atazanavir drug	0.2 to 2.7 μg/g (drag)	[19]
Kinetic	Hydrazine, MMH	Thiophene-3-carboxaldehyde (3-Thienaldehyde)	not specified	$0.1 \cdot 10^{-3}$ – 0.1	[10]
	Hydrazine, MMH	Butenone (E)-1,1,1-trifluoro-4-(3-thienyl) (CF_3 enone)	not specified	$0.1 \cdot 10^{-3}$ – $1 \cdot 10^{-3}$	[10]
	Hydrazine, MMH	2,4-dinitro-1-chloro-benzene (CDNB)	not specified	0.1 – 0.004	[10]
	Phenyl-hydrazine	Meta cresol purple (MCP), periodate, bromide ions	Water samples	0.032 – 0.32	[20]
	Hydrazine	Thionine-bromate	Cooling tower water samples	0.8 – 23.04	[21]
	Hydrazine and isoniazid	Iron (III), 2,2'-bipyridine (Bpy)	Izoniazid drug	0.08 − 5.76, 1.024 − 80	[23]
	Hydrazine	Victoria Blue 4-R, $KBrO_3$	Water-steam system and Isoniazid tablets	0.03 - 1.4	[22]
Flow injection	Hydrazine	p-Dimethylamino-benzaldehyde (pDMAB)	Stream of nuclear fuel reprocessing	0.05 - 10	[26]
	Phenyl-hydrazine	Thionine	Human serum and water samples	0.0016 – 0.0192	[28]

Flow injection	Hydrazine	Vanillin (3-methoxy-4-hydroxylbenzaldehyde)	Water samples	0.002 – 1.5	[29]
	Hydrazine	p-Dimethylamino-benzaldehyde (pDMAB)	Environmental water	0.002 – 0.1 and 0.1 – 1.500	[27]

2.1. Kinetic methods

Recently, the application of inhibition effects of hydrazines with different reagents in the kinetic spectrophotometric methods was reported. These methods are based on the influence of hydrazine and its derivatives on the rate of oxidation of active in UV-Vis region indicator by inhibiting it.

It was established that phenylhydrazine demonstrates inhibition effect on catalytic reaction due to possible perturbation in the catalytic cycle via reaction with Br_2, periodate, and/or other reaction intermediates [20]. The inhibition effect was shown in reaction between meta-cresol purple (MCP) and periodate in the presence of bromide ions. The reaction was monitored spectrophotometrically by measuring the change in absorbance of MCP at 525 nm. The calibration graph was linear in the range of 1.0-10.0 μM. The detection limit (3σ) was 0.020 μM.

Kinetic methods based on inhibition effect of hydrazine on thionine-bromate system in sulfuric acid media and on Victoria Blue 4-R – bromate system were developed and validated for the determination of hydrazine. The calibration curve was linear in the concentration range of 0.8–23.0 ppm and of $9.36 \cdot 10^{-7}$–$4.37 \cdot 10^{-5}$ mol dm^{-3}, respectively. The detection limit of the reported methods is 0.22 ppm and $9.98 \cdot 10^{-8}$ mol·dm^{-3}, respectively [21, 22].

Thiophene-3-carboxaldehyde (3-thienaldehyde) and 3-butenone (E)-1,1,1-trifluoro-4-(3-thienyl) (CF3 enone) in concentration range of 0.1 mM to 0.1 M for 3-thienaldehyde and 0.1 mM to 1 mM for CF_3 enone were used for the determination of hydrazines (Fig. 1, 2). LOQ for 3-thienaldehyde were found to be 0.2 mM (hydrazine) and 0.1 mM (MMH). For CF_3 enone, LOQ are 0.007 mM (hydrazine) and 0.01 mM (MMH) [10].

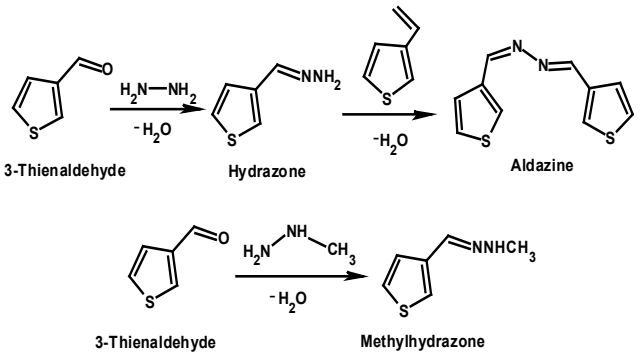

Figure 1. Interaction of 3-thienaldehyde with hydrazine and MMH [10].

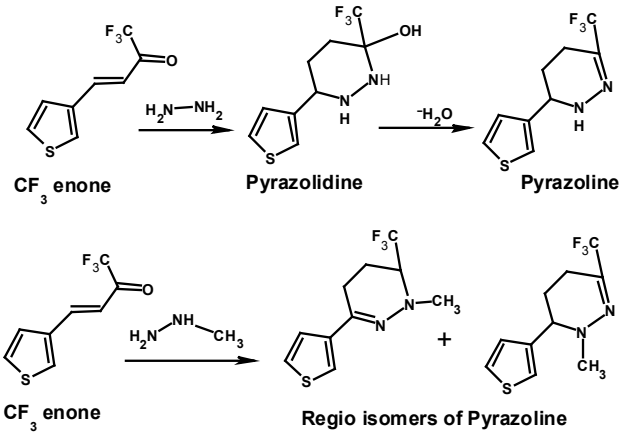

Figure 2. Interaction of CF_3 enone with hydrazine and MMH [10].

Kinetic spectrophotometric method based on the reaction of propellant grade hydrazines and its derivatives with 1-chloro-2,4-dinitro-1-chlorobenzene (CDNB) incorporated in a solution matrix of polyaniline-Emaraldine Base (Pani-EB) is described in [10] (Figure 3).

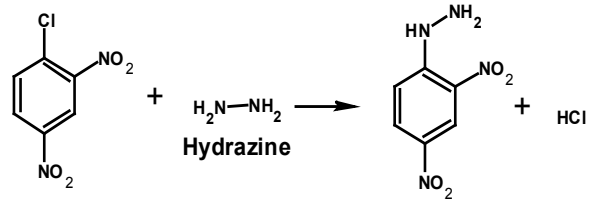

Figure 3. Reaction of hydrazine with CDNB with release of HCl [10].

Strong acid protonates Pani (EB-Blue) to form Pani Emeraldine salt (ES-Green) (Figure 4). A kinetic study based on the gradual decrease in absorbance at 626 nm for both nano and conventional Pani–CDNB systems was carried out at 50 ˚C and 60 ˚C under optimized conditions in the dynamic concentration range of 0.1–0.004 M.

Application of kinetic spectrophotometric method that comprises H-point standard addition method (HPSAM) and partial least squares (PLS) calibration was described in [23] for the determination of hydrazine and isoniazid (INH).

The method is based on the difference observed in the rate of iron (III) reduction with hydrazine and INH in the presence of 2,2'-bipyridine (Bpy) and

the subsequent complex formation between the resulted Fe^{2+} and Bpy in a solution containing sodium dodecyl sulfate (SDS) as a micellar medium. INH and hydrazine can be simultaneously determined in the range of 0.08−6.0 and 1.0−80.0 ppm respectively.

All described kinetic spectrophotometric methods are compared in the table 1.

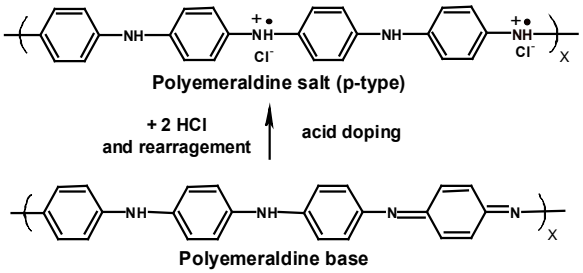

Figure 4. Conversion of Pani-EB to Pani-ES on acidic doping [10].

2.2. Flow injection methods

Flow-based procedures have fulfilled several principles of green chemistry [24]. From a theoretical point of view, the excess of a reagent required for chemical derivatization is lower than in the batch mode. The first principle is also kept by replacing toxic chemicals, drastically minimizing reagent amounts and waste generation or even allowing reagent recycling and reuse. Sample treatment is usually simpler and faster, thus, unnecessary chemical waste is avoided. Real-time monitoring of industrial or environmental processes is also feasible satisfactory. In addition, potential risks to analysts are reduced by sample processing in a closed system and by automation which minimizes exposition to toxic substances and makes the analytical operation less dependent on operator [25]. The main drawbacks of flow injection are its selectivity and sensitivity that do not differ from spectrophotometry and low yield of the product of analytical reaction. The choice of reagent and conditions of the measurements can affect the selectivity and sensitivity of flow injection methods.

Hydrazine is also determined in the aqueous streams by liquid chromatography coupled with UV-visible detector [26] and direct spectrophotometric method [27] with the application of flow injection method. The methods are based on the formation of yellow coloured azine complex by reaction of hydrazine with pDMAB. The formed yellow colored complex is stable in acidic medium and has a maximum absorption at 460 nm. The presence of uranium does not interfere with the analysis of hydrazine solution. Under optimal conditions the absorbance intensity linearly increased with the concentration of hydrazine in the range 0.05-10 ppb and 2.0–100.0 ppb, respectively. The experimental detection limit is 0.05 and 0.016 ppb, respectively. The sampling frequency is 15 and 24 samples·h^{-1} and the relative standard deviation was 2.1% for 0.05 mg·L^{-1} and 0.38% for 0.1 ppm, respectively. These methods are suitable for automatic and continuous analysis and are successfully applied for determination of hydrazine in aqueous stream of nuclear fuel reprocessing and in river, pond and waste water.

A flow injection colorimetric procedure for the determination of phenylhydrazine based on its reaction in sulfuric acid with thionine and sodium nitrite was elaborated. Reaction was monitored spectrophotometrically by measuring thionine absorbance at λ_{max} = 602 nm. A standard or sample solution was injected into the sulfuric acid stream, which was then merged with sodium nitrite stream and thionine stream. A linear calibration graph was obtained in the range 0.05–0.60 ppb, and the detection limit was 0.027 ppb. The proposed method has been satisfactorily applied to the determination of phenylhydrazine in human serum and water samples [28].

Flow injection spectrophotometric method was proposed in [29] for online determination of hydrazine. It is based on the condensation reaction of hydrazine with vanillin (3-methoxy-4-hydroxylbenzaldehyde). The resulting yellow colored product is stable in acidic medium and has maximum absorbance at 410 nm. Under optimal conditions the absorption intensity dependent on the concentration of hydrazine increased linearly in the range of 2–1500 ppb with a correlation coefficient of R^2 = 0.9997 and detection limit 0.70 ppb. The sampling frequency is 20 samples·h^{-1}, the relative standard deviation is 0.98% (n = 11) at 100 ppb of hydrazine. This proposed method is suitable for automatic and continuous analysis and is applied successfully for determination of hydrazine in river, pond, well, real boiler and waste water samples with the recoveries in the range of 99.0%–104.6%. Comparison of flow injection methods is presented in Table 1.

3. Visual tests and optical sensors

Sensor is one of the most crucial analytical technologies and tools for detecting toxic chemicals in the environment. Therefore, there is the need to have an effective and sensitive method for hydrazine detection. Recently, several attempts have been made to develop rapid, sensitive, and selective visual tests for the determination of hydrazine.

In comparison to spectrophotometry, fluorescent method is characterized by higher sensitivity and lower detection limits. Thus, most of recent works focused on synthesis of fluorescent reagent, and many of them were used in fluorescent sensors.

The development of sensitive and selective colorimetric sensors is highly demanded due to their simplicity, rapidity, precision and usage of common laboratory equipment. Recently great efforts were made in order to develop a sensor for monitoring harmful materials with the aim to protect the health of human and environments.

Optical sensors based on nanoparticles as well as colorimetric and fluorescent sensors are worked out nowadays.

3.1. Optical sensors based on nanoparticles

Among many materials, gold nanoparticles (AuNPs) are considered to be the most perspective candidates for the determination of hydrazines with the regard to their unique optical properties. Intrinsically strong surface plasmon resonance (SPR), extremely high extinction coefficients in the visible wavelength range caused remarkable progress in the design of AuNPs-based colorimetric biosensors. There are some colorimetric methods based on gold nanoparticles for determination and detection of hydrazine [30-36].

A colorimetric method for hydrazine detection using tryptophan-caped gold nanoparticles (Trp-AuNPs) was developed in [30]. Tryptophan (Trp) is a protein with amino group which can reduce chloroauric acid ($HAuCl_4$) to AuNPs and modify the surface of AuNPs simultaneously. The Trp-AuNPs can be used to detect hydrazine quantitatively. It demonstrated different responses to various concentrations of hydrazine in aqueous solution based on the color change of Trp-AuNPs from red to blue induced by aggregation. The application for analysis of water samples proved the feasibility of proposed technique. Size of AuNPs that is caused by pH of solution, concentration of Trp and the reaction time influences the sensitivity of detection. The limit of detection of hydrazine is 1 μM. A linear correlation existed between the absorption ratio A_{540} and the hydrazine concentration in the range from $7.57 \cdot 10^{-6}$ to $2.01 \cdot 10^{-3}$ M. The authors expect their approach to have wide-ranging applications in the developing region for monitoring water quality in some areas.

The development of a simple and rapid colorimetric method of detection of low levels of hydrazine in boiler feed water using label-free aggregation-based gold nanoparticles as probe is reported in [31]. Proposed approach is based on optical properties of gold nanoparticles dependent on distance. Hydrazine can induce the aggregation of gold nanoparticles rapidly, thereby resulting in color change from red to blue (or purple). Concentration of hydrazine can be determined by naked eye or by UV–vis spectrometer. Calibration curve was linear in concentration range from $1.0 \cdot 10^{-11}$ to $1.0 \cdot 10^{-7}$ M of hydrazine. Limit of detection for hydrazine was $1.0 \cdot 10^{-12}$ M. The method is rather simple, and the entire process including sample preparation takes only 15 min at room temperature. The proposed method is especially useful for on-site screening of hydrazine levels in boiler feed water.

A colorimetric sensor based on gold nanoparticles for determination of hydrazine is presented in [32]. The reduction of $AuCl_4^-$ to gold nanoparticles by hydrazine produced very intensive surface plasmon resonance peak of AuNPs. The formation of gold nanoparticles as a result of the redox reaction in water samples was identified by measuring the localized surface plasmon resonance (LSPR) absorption. LSPR intensity displays linear response to the increase of hydrazine concentration in the range from 6.0 to $40.0 \cdot 10^{-6}$ M, with a detection limit of $1.1 \cdot 10^{-6}$ M. The relative standard deviation for determination of 10×10^{-6}M and $28 \cdot 10^{-6}$ M of hydrazine was 3.2% and 0.68% (n = 6), respectively. Visual detection of hydrazine based on color change was performed. It was used for analysis of hydrazine in industrial water (boiler and cooling water) and river water.

A colorimetric detection of hydrazine based on formation of size-controlled amidosulfonic acid capped by gold nanoparticles (AA-AuNPs) was developed in [33]. Hydrazine served not only as a target analyte but also a reductant to react with chloroauric acid ($HAuCl_4$). In order to obtain size-controlled gold nanoparticles (AuNPs) the amidosulfonic acid (AS) was used as a stabilizer. In the presence of AS different aggregation states of AuNPs, which exhibited distinct color changes, were obtained by varying the concentration of hydrazine. Furthermore, the changes of color resulted in different ultraviolet visible (UV-Vis) absorptions, which realized quantitative analysis of hydrazine. The results performed as the ratio of absorbance intensities at 540 nm and 225 nm (A_{540}/A_{225}) had a wide linear range from $1.0 \cdot 10^{-7}$ to $2.53 \cdot 10^{-4}$ M (r = 0.9915) and low detection limit of $8.53 \cdot 10^{-8}$ M.

A visual detection of hydrazine hydrate using Au nanoparticles-based colorimetric sensing system (ANCSS) is reported in [34]. This approach is based on the hydrogen bonding recognition and the modality change of hydrogen bonding from ‘‘linear’’ (simple hydrogen bond interactions) to ‘‘nonlinear’’ (a complicated hydrogen bond network) between modified Au nanoparticles (AuNPs). A wide linear response was obtained in concentration range $5 \cdot 10^{-8}$–$2.75 \cdot 10^{-5}$ M (R = 0.99) and LOD could be decreased to 2.5 ppb within 30 seconds.

Prussian blue nanoparticles (PBNPs) were used in optical sensor for colorimetric detection of hydrazine in pharmaceuticals in [35]. The method is based on the reduction of Fe(III) to Fe(II) by hydrazine in the presence of ferricyanide while preparing PBNPs in a slightly acidic medium. UV-vis spectrophotometry was used to monitor the changes of the absorption intensity of prussian blue nanoparticles. These nanoparticles exhibited a strong UV-vis extinction band at 700 nm. Change in color of the solution, which is directly related to the analyte concentration, could be easily observed with the naked eye in the presence of a sub-ppm level of hydrazine. The effect of several reaction variables on the rate of the PBNP formation was studied and optimized. A linear relationship between absorbance intensity of PBNPs and the concentration of hydrazine over a range of 0.4 μg mL^{-1} to 2.0 ppm with correlation coefficient (R^2) of 0.9967 was observed; moreover, the detection limit was found to be 0.33 ppm. The proposed

method was successfully applied for the determination of hydrazine concentration in pharmaceutical samples with satisfactory results.

An indirect colorimetric method for spectrophotometric determination of hydrazine, phenylhydrazine and isoniazid was elaborated in work [36]. Reduction of silver ions to silver nanoparticles (AgNPs) by these analytes in the presence of polyvinylpyrrolidone (PVP) and cetyltrimethylammonium chloride (CTAC) as a stabilizer underlies the proposed method. The changes in plasmon absorbance of the AgNPs at λ = 415 nm in the presence of PVP were proportional to concentration of hydrazine, phenylhydrazine and isoniazid in the ranges of 4.0–150.0 μM, 1.0–55.0 μM, and 2.0–30.0 μM, respectively, and the detection limit obtained was 0.79 μM. In the presence of CTAC, the linear ranges were 0.5–10.0 and 10.0–300.0 μM for hydrazine, 1.0–40.0 μM for phenylhydrazine, and 0.2–10.0 and 10.0–90.0 μM for isoniazid, and the detection limit was 0.12 μM. The method has been applied for determination of these analytes in different real samples such as boiler feed water and pharmaceuticals. The comparison of visual methods that are based on application of nanoparticles for detection of hydrazine is presented in Table 2.

Table 2. Comparison of visual test techniques and optical sensors for detection of hydrazine and its derivatives.

Reagent	Object	λ_{max}, nm	LOD, ppm	Analytical range mol/L	Ref.
Tryptophan-caped gold nanoparticles (Trp-AuNPs)	Water samples	540	0.032	0.024 – 64.32	30
Gold nanoparticles	Boiler feed water	688	0.000032	$3.2\cdot10^{-7}$ – 0.0032	31
Gold nanoparticles (AuNPs)	Water samples	580	0.032	0.192–1.28	32
Amidosulfonic acid capped gold nanoparticles (AA-AuNPs)	Water samples	A_{540}/A_{225}	0.003	0.0032 – 8.1	33
Au nanoparticles-based colorimetric sensing system (ANCSS)	not specified	519	0.0025	0.0016 – 0.88	34
Ferric ions+ ferricyanide ion (PBNPs)	Pharmaceutical samples	700	0.4	$1.25\cdot10^{-5}$ – $6.25\cdot10^{-5}$	35
Merocyanine 6- pyrazolinyl merocyanine 6- pyrazolinyl	Hydrazine gas and water samples	-	-	$2\cdot10^{-5}$ –$180\cdot10^{-5}$	38
4-Decyloxybenzaldehyde (DBA)	Hydrazine vapors	514.5	30	$7.8\cdot10^{-4}$ – 0.016	39
Pentacenediquinone (PDQ)	Hydrazine vapors	1310 -1550	0.2	$6.25\cdot10^{-6}$ – $1.25\cdot10^{-3}$	40
Silver ions+polyvinylpyrrolidone (PVP)	Boiler feed water and tablet	415	0.0025	0.128 – 4.8	36
Silver ions+cetyltrimethylammonium chloride (CTAC)	Boiler feed water and tablet	415	0.0025	0.016 – 0.32 0.32 – 9.6	36
p-(Dimethylamino)benzaldehyde	Water samples, cells	-	0.1	$3.12\cdot10^{-4}$ – $9.4\cdot10^{-3}$	40
Trifluoroacetyl acetonate naphthalimide	Hydrazine vapors, cells	501	0.0032	$1.0\cdot10^{-6}$–$5\cdot10^{-6}$	46
Tetraphenylethene-functionalized poly(arylene ynonylene)	not specified	540	320	$10\cdot10^{-6}$ – $400\cdot10^{-6}$	47
2-(4-Methoxyphenyl)-4-oxo-4H-chromen-3-yl acetate (MOCA)	Cells	540	0.32	$1.0\cdot10^{-6}$ – $50\cdot10^{-6}$	48
Resorufin	Cells	584	320	$10\cdot10^{-6}$ – $200\cdot10^{-6}$	49
NIR-N_2H_4 (7-hydroxycoumarin)	Serum, cells	725	0.0023	$1.0\cdot10^{-6}$ – $5.0\cdot10^{-4}$	50
Heptamethine cyanine dye derivative	Cells	600	0.0081	-	51
3,6-Diacetoxyfluoran (FDA)	Water samples	515	0.1	1.25 – 25.00 μM	52

Levulinated hydroxycoumarin	Cells	425	0.08 ppm	$0.1 \cdot 10^{-5}$ – $14 \cdot 10^{-5}$	53
7-Diethylamino1,4-benzoxaz-in-2-one (DEAB)	Cells	460	0.0022	0.07 – 0.37 μM	54
Malononitrile group and phenothi-azine dye	Cells	490	0.4	$5.0 \cdot 10^{-6}$ – $20.0 \cdot 10^{-6}$	55
2-(4-((4-(Benzo[d]thiazol-2yl) phenyl)ethynyl) benzylidene)malononitrile	Water samples	410-700	0.00011	—	56
Sodium dioctyl sulfosuccinate (AOT)	not specified	~780	0.24	0.05 – 5.00 ppm	43

3.2. Optical sensors based on colorimetric detection

In recent years, colorimetric methods have attracted much attention due to their low cost, simplicity and functionality. Since color changes can be observed by naked eye, colorimetric sensor does not require expensive or sophisticated instrumentation and may be applied to field analysis and point-of-care diagnosis. These methods have shown great advantages over conventional assays, particularly in sensitivity, selectivity and practicality [37].

The merocyanine, a sensor for hydrazine hydrate in aqueous ethanolic medium and for hydrazine gas, was elaborated in [38]. 1,2,2,4-Tetramethyldihydro quinoline (TMDQ) is formylated in 6th position and the resulting quinolone aldehyde is condensed with 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one to obtain a merocyanine 6-pyrazolinyl TMDQ. The merocyanine detects hydrazine hydrate in less than 5 s in the presence of other amines, anions and metals in the range of $2 \cdot 10^{-5}$ to $180 \cdot 10^{-5}$ M of hydrazine hydrate. The detection can be done simply by naked eye and quantification can be done by absorbance/ fluorescence spectroscopy. Hydrazine hydrate as well as hydrazine gas can be detected by the TLC plate technique.

A liquid crystal (LC) based sensor to detect hydrazine vapor has been developed in [39]. The LC 4-pentyl-4-biphenylcarbonitrile (5CB) doped with 0.5 wt% 4-decyloxybenzaldehyde (DBA) shows dark to bright optical texture upon exposure of hydrazine vapours as revealed by polarizing optical microscopy under crossed polarizers. The hydrazine interacts with the doped DBA and forms diimine compound which disrupts the orientation of aligned 5CB. The interaction between DBA and hydrazine has been also studied by Raman spectroscopy. The lowest detection limit for this sensor is ~30 ppm.

Couple of years ago the development of a reversible fiber optic leak sensor capable of detecting the traces of hydrazine was reported in [9, 40]. The sensor operates in the lowest attenuation wavelength range of commercial silica fibers. The sensing material utilized in this sensor is a mix of organic compounds that contains pentacenediquinone (PDQ) as an active sensing element. The index of refraction of this mix is adjusted to closely match that of fiber's silica core. In the absence of hydrazine this mix exhibits a weak absorption in the near-infrared. When the PDQ reacts with hydrazine, oxygen atoms from the PDQ are replaced by a molecule of hydrazine resulting in water as a by-product. This replacement significantly increases the absorption of the mix specifically at wavelength between 1310 and 1430 nm. This absorption was found to be proportional to hydrazine gas concentration. The reaction however is a self-reversible i.e. in the presence of water; the by-products of the reverse reaction would be PDQ and hydrazine.

Colorimetric sensor array for the detection and identification of toxic industrial chemicals (TICs) has been developed in [41]. The sensor consists of a disposable array of cross-responsive nanoporous pigments whose colors are changed by diverse chemical interactions with analytes. Clear differentiation among 20 different TICs has been easily achieved at both their IDLH (immediately dangerous to life or health) concentration within 2 min of exposure and PEL (permissible exposure limit) concentration within 5 min of exposure with no errors or misclassifications. Detection limits are generally well below the PEL (in most cases below 5% of PEL) and are typically in the low ppb range. The colorimetric sensor array is not responsive to changes in humidity or temperature over a substantial range. The printed arrays show excellent batch to batch reproducibility and long shelf life (greater than 3 months).

The sensor was constructed by immobilizing a reagent on TLC (Thin Layer Chromatography) paper [42]. This procedure is based on chromogenic reaction of hydrazine with p-(dimethylamino) benzaldehyde (reagent) and formation of red colored product followed by scanner-based detection (Figure 5). Changes in RGB values of color spots on TLC strips create a pattern. The obtained pattern was analyzed by MATLAB software. The results are linear in concentration range 10–300 $\mu g \cdot mL^{-1}$ of hydrazine. Detection limit is 0.1 $\mu g \cdot mL^{-1}$. Parameters such as pH and concentration of p-(dimethylamino)benzaldehyde were optimized. The proposed sensor was applied for the determination of hydrazine in bovine serum and tap water.

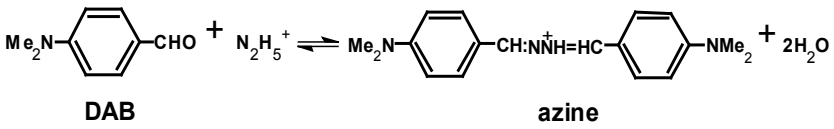

Figure 5. Condensation reaction of p-(dimethylamino)-benzaldehyde (DAB) with hydrazine [42].

Chemical sensor for hydrazine detection was developed using polyaniline (PAni). The sensor response was analyzed using UV–Vis spectrometer, where there is notable decrease in intensity at ~780 nm after the PAni was exposed to hydrazine. PAni thin film showed a tolerable limit of detection of 0.24 ppm [43].

3.3. Fluorescence sensors

Recently the fluorescence spectroscopy has been used widely for detection of various analytes because of its high sensitivity, specificity, handiness, relatively low cost and real-time monitoring [44, 45]. A lot of attention is paid to the development of approaches for the determination of hydrazines using fluorescent reagents [46]. In acetonitrile solution trifluoroacetyl acetonate naphthalimide derivative (TFAANI) reacts selectively with hydrazine to give a five-membered ring. This leads to OFF–ON fluorescence with a maximum intensity at 501 nm as well as easily discernible color changes. Based on a readily discernible and reproducible 3.9% change in overall fluorescence intensity, the limit of hydrazine detection is 3.2 ppb (0.1 μM). This reaction is selective for hydrazine in the presence of other amines, including NH_4OH, NH_2OH, ethylenediamine, methylamine, n-butylamine, piperazine, dimethylamine, triethylamine and pyridine. Environmentally abundant metal ions do not interfere with the determination of hydrazine. When supported on glass-backed silica gel TLC plates, compound 1 acts as a fluorometric and colorimetric probe for hydrazine vapor at a partial pressure of 9.0 mm Hg, with selectivity over other potentially interfering volatile analytes, including ammonia, methylamine, n-butylamine, formaldehyde, acetaldehyde, H_2O_2, HCl, and CO_2 being observed. Probe 1 can also be used for the detection of hydrazine in HeLa cells without appreciable interference from other biologically abundant amines and metal ions.

A high molecular weight poly(arylene nonylene) with an aggregation-enhanced emission characteristic was synthesized [47]. Its emission can be turned 'on' by hydrazine, as well as 'off' by picric acid, demonstrating the first fluorescent sensor that works for both hydrazine and explosive agents detection (Figure 6).

Detection of hydrazine in environment and in vivo is of great significance for environmental protection and biotoxic evaluation. A flavonoid-based sensor 2-(4-methoxyphenyl)-4-oxo-4H-chromen-3-yl acetate (MOCA) was developed to monitor hydrazine with detection limits 0.32 ppm and linear range from 0 to 50 μM [48]. Upon addition of hydrazine, the fluorescence intensity of MOCA greatly enhanced and showed linear response to the concentration of hydrazine. Other amine-containing species or commonly encountered ions barely interfered with the detection of hydrazine. Furthermore, this sensor could visualize the hydrazine in stem cells and zebrafish, thus providing a powerful fluorescent imaging tool for tracking hydrazine in vivo.

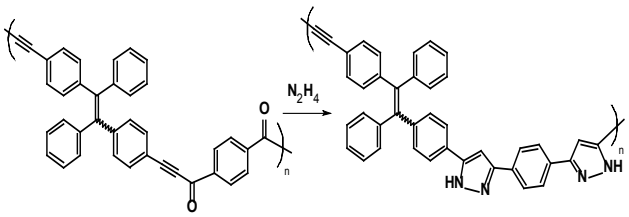

Figure 6. Reaction of tetraphenylethene-functionalized poly(arylene ynonylene) with hydrazine [47].

A novel colorimetric and red-emitting fluorescent probe HFH based on resorufin platform was developed for hydrazine detection [49]. This OFF–ON fluorescent probe shows a large (117 nm) red-shifted absorption spectrum and the color changes from colorless to red upon addition of hydrazine in the aqueous solution, which can serve as a "naked-eye" probe for hydrazine. Moreover, this probe also shows a significant fluorescence increase (~16 folds) and excellent linear relationship at physiological pH. Utilizing this sensitive and selective probe, the authors have successfully detected hydrazine in living cells.

A near-infrared (NIR) fluorescent probe for monitoring hydrazine in blood samples and live cells was designed and synthesized [50]. Compound NIR-N_2H_4 (Figure 7) is a candidate for fluorescent hydrazine probes with emission in the NIR region for detecting hydrazine in serum and cell imaging of hydrazine. The rational design of the NIR probe NIR-N_2H_4 is based on careful considerations. This method shows linear dependence in the range from 1.0 to $5.0 \cdot 10^2$ μM. The detection limit of hydrazine is 2.3 ppb at pH 7.0, HEPES/CH_3CN (7:3).

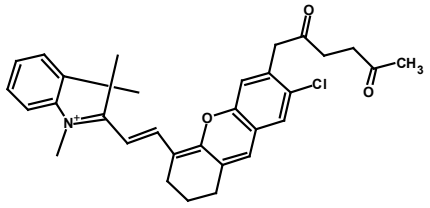

Figure 7. NIR fluorescence turn-on hydrazine probe [50].

Based on modulation of the conjugated polymethine π-electron system of a cyanine dye derivative, a ratiometric NIR fluorescent probe (Cy7A) for hydrazine has been designed and synthesized [51]. Cy7A can be selectively hydrazinolysized with great changes in its fluorescent excitation/emission profiles, which makes it possible to detect N_2H_4 in water samples and living cells, visualize N_2H_4 in living mice. Cy7A showed a ratiometric fluorescence response that was selective for hydrazine over other species with a detection limit of 0.81 ppb.A fluorescent probe capable of reliable detection of hydrazine under environmentally friendly conditions with high specificity and sensitivity was developed in [52]. 3,6-Diacetoxyfluoran (FDA), a readily commercially available compound, is explored for fluorescence "switch-on" detection of hydrazine. FDA can undergo hydrazinolysis and transform into fluorescein in aqueous solution at neutral pH, resulting in distinct optical changes from colorless to green and "switch-on" fluorescence which allows to establish a new method for sensitive detection of hydrazine (Figure 8). Under optimum conditions described in this work, the enhancement of fluorescence at 515 nm was linearly proportional to the concentrations of hydrazine ranging from 1.25 to 25.00 μM with a correlation coefficient of $R^2 = 0.9959$ and a detection limit as low as 31 nM. The relative standard deviation of twelve replicate measurement samples was 5.4% for 12.5 μM hydrazine. The proposed method is convenient, low cost and free of complex equipment, making it possible to successfully determine hydrazine in four real samples containing distilled water, tap water, isoniazid and plasma. Furthermore, the hydrazine probe would be a promising candidate capable of naked-eye visualization of gaseous hydrazine by simple operations.

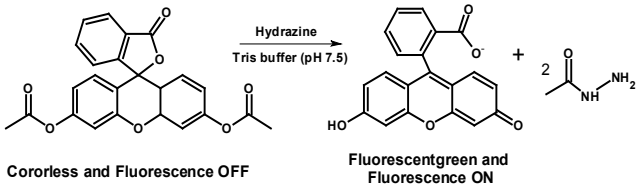

Figure 8. Representative reaction mechanism of FDA with hydrazine [52].

Chemosignaling of hydrazine by selective deprotection of levulinated coumarin was investigated in [53]. In the presence of hydrazine, levulinated coumarin was selectively deprotected, resulting in chromogenic and fluorescent turn-on type signaling. The selective naked-eye detectable signaling of hydrazine was possible in the presence of representative metal ions and common anions in an aqueous environment. Detection limit of levulinated hydroxycoumarin for the determination of hydrazine was estimated to be 2.46 μM (0.08 ppm) in a 30% aqueous DMSO solution. The calibration graph was linear in the range of $0.1 \cdot 10^{-5}$-$14 \cdot 10^{-5}$ M hydrazine.

3.4. Fluorescence sensors based on intramolecular charge transfer (ICT)

A fluorophore 7-diethylamino1,4-benzoxazin-2-one (DEAB), an ICT-based ratiometric probe that can selectively detect traces of hydrazine in vitro was investigated in [54]. The probe exhibits hydrazine induced changes in the intensity ratios of both absorption and emission spectra. The significant changes in fluorescence color were observed by naked eye. Live-cell imaging experiments establish the utility of this probe for tracking hydrazine in live cells (Figure 9).

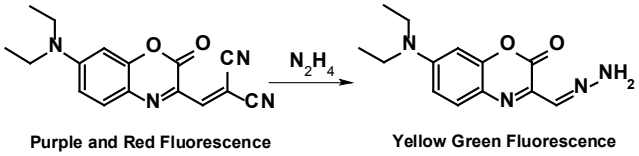

Figure 9. The proposed mechanism of the response of DEAB to hydrazine [54].

The UV-vis spectra of probe exhibited a maximum absorption at 598 nm. Upon addition of hydrazine, the absorption at 598 nm evidently decreased, whereas a new absorption peak appeared at 460 nm with an isobestic point at 510 nm. A linear relationship was observed between the fluorescence intensity and hydrazine amount in the range of 0.07–0.37 μM.

ICT-based fluorescence sensor was elaborated in [55] for hydrazine determination in live cells and in live fish. The sensing mechanism is rationalized with the aid of TD-DFT (time-dependent density functional theory) calculations. As presented in scheme 18, sensor 1 was synthesized by introduction of malononitrile group as the electron acceptor and phenothiazine dye (compound 2) as the electron donor to form an ICT process. With the introduction of hydrazine, a specific reaction between the arylidene malononitrile and hydrazine group occurred and produced hydrazone, which affected the intramolecular electron density distribution, followed by the change of absorption and emission (Figure 10). Huge fluorescence enhancement (about 80-fold) provides a significant property for hydrazine detection. Furthermore, the proposed sensor can penetrate into live cells and especially live fish.

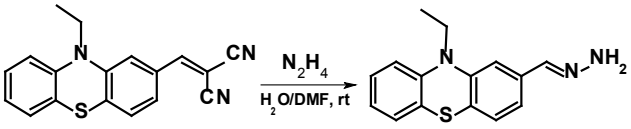

Figure 10. The proposed mechanism for the response of fluorescent probe to hydrazine [55].

A fluorescent and colorimetric probe based on the reaction and intramolecular charge transfer (ICT) effect is designed and synthesized in work [56]. The probe responds rapidly toward hydrazine and exhibits distinct

color changes from yellow to colorless, indicating its use as a color indicator for hydrazine (Figure 11). Moreover, the probe also shows a significant broad band fluorescence (410-700 nm) enhancement by ~120-fold after the addition of hydrazine. With a detection limit as low as 0.11 ppb, the probe can detect hydrazine in a wide concentration range because of the blunted sensing functional group. The contrast test shows almost no interruption from common elements in water, suggesting the high selectivity of this probe toward hydrazine. The theoretical calculation based on density functional theory (DFT) is also performed and two different ICT modes are found. This hydrazine probe was suggested as a candidate applicable in environment protection, water treatment and safety inspection.

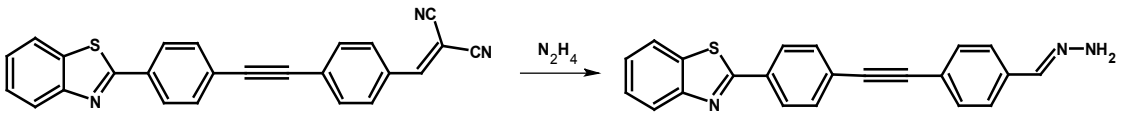

Figure 11. The proposed sensing mechanism of probe 2-(4-((4-(benzo[d]thiazol-2-yl)phenyl)ethynyl)-benzylidene) malononitrile (BP) [56].

4. Conclusion

Detection of hydrazine and its derivatives in environment and in vivo is of great significance for environmental protection and evaluation of biotoxicity. Visual test methods and colorimetric sensors were proved to be simple and applicable in real life conditions. Fluorescence sensors with turn-on mechanism are perspective for determination of hydrazine and its derivatives in different objects, including air. Fluorescent ratiometric sensors are highly selective – metals and organic compounds do not interfere with the determination of hydrazines in biological objects, specifically in cells. The problem of hydrazines determination remains actual because synthesis routes of most of fluorescent and spectrophotometric reagents are complicated. Thus, simple techniques for development of optical sensors which will be characterized by good figures of merit are encouraged.

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